2001

Influence of short-term endurance exercise training on heart rate variability

Clarence Matthew Lee
Louisiana State University and Agricultural and Mechanical College

INFLUENCE OF SHORT-TERM ENDURANCE EXERCISE TRAINING ON HEART RATE VARIABILITY

A Dissertation

Submitted to the Graduate Faculty of the
Louisiana State University and Agricultural and Mechanical College
in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy
in
The Department of Kinesiology

by
Clarence Matthew Lee
B.S., University of Southwestern Louisiana, 1995
December, 2001

Acknowledgements

I would like to acknowledge the support of all faculty and staff in the Department of Kinesiology at Louisiana State University. I am especially grateful to my major advisor and mentor, Dr. Robert H. Wood, for his endless hours of support, inspiration, and guidance throughout my graduate career. Also of special recognition are Dr. Michael A. Welsch and Dr. Arnold G. Nelson, whose contributions to my knowledge in the field of exercise physiology have been invaluable. I would further like to thank the other members of my graduate committee, Dr. Joseph Woodring and Dr. Doo-Youn Cho, for their helpful comments and discussion. I also extend a special thanks to Claire Hutchinson for her assistance in the collection of data for my dissertation.

I am eternally grateful to my parents, Mike and Barbara Lee, for providing me with the support and guidance I needed, and for teaching me the importance of getting a quality education. I especially thank my best friend and companion for life, Kristi Metoyer, who has been by my side throughout my graduate career and will be forever. Furthermore, I am grateful to my brother Michael, and my grandparents Marjorie Kohnke and Willard Lee, and the late, Clarence Kohnke and Gloria Lee. Most of all, I would like to thank God for giving me the strength and guidance to excel throughout my academic and personal life.

Table of Contents

List of Tables

List of Figures

Abstract

The purpose of this investigation was to determine if 8 exercise endurance training (ET) sessions over 2 weeks significantly alters cardiac autonomic modulation, as measured by heart rate variability (HRV). Twenty-four college-aged males were recruited for this study and were randomized into either an exercise group (EX; n=12) or a control group (CT; n=12). EX underwent 2 weeks of ET on a cycle-ergometer (frequency: four times/week; duration: 40 minutes; intensity 80-85% $HR_{reserve}$), whereas CT was instructed not to alter their previous level of physical activity. Five-minute ECG tracings were collected for HRV under the following conditions: 5 minutes of paced breathing at a frequency of 12 breaths/minute (PB), 5 minutes of spontaneous breathing (SB1), 5 minutes of 70-degree head-up tilt on a tilt table (TILT), and a second 5-minute period of spontaneous breathing (SB2). The data were collected on 5 occasions (Test 1-Test 5) during a 2-week period. HRV was reported as the standard deviation of RR intervals, and as normalized units (NU) of the natural logarithm of high- and low-frequency power (lnHF and lnLF). A mixed-model analysis of variance (ANOVA) with repeated measures was used to evaluate any Group X Time interaction, or main effects of Group or Time on HRV. Alpha was set at 0.05. EX exhibited a significant increase in peak oxygen consumption (8%), whereas this parameter was unchanged in CT. During PB, ANOVA revealed a Group X Time interaction such that EX exhibited decreases in lnLFNU (2.89 vs. 3.45 ln%) and lnLF/lnHF (0.82 vs. 0.90) during Test 5 compared to Test 1, while there were no such differences across time in CT. Additionally, there was a Group X Time interaction during TILT such that EX exhibited lower lnLFNU (4.12 vs. 4.42 ln%) and lnLF/lnHF (1.12 vs. 1.46), and greater lnHFNU (3.52 vs. 2.53 ln%) during Test 5 compared to Test 1, while these indices were unchanged across time in CT. These data suggest that 8 ET

sessions over 2 weeks increases vagal modulation of the heart. Furthermore, these data suggest that it takes at least 8 ET sessions to induce such changes.

Introduction

Heart rate variability (HRV) has gained recent popularity as a noninvasive index of cardiac autonomic modulation and can provide a reliable measure of cardiac sympathovagal balance (Berntson et al. 1997). More specifically, power spectral analysis of HRV provides a marker of cardiac autonomic balance by separating the beat-to-beat fluctuations in heart rate into those occurring at lower frequencies (LF: 0.04 – 0.15 Hz) and those occurring at higher frequencies (HF: 0.15 – 0.40 Hz). Those fluctuations in the HF range appear to mainly reflect parasympathetic, or vagal, modulation of the heart, whereas those in the LF range are believed to reflect both sympathetic and parasympathetic influences (Akselrod et al. 1981; Pagani et al. 1986). A list of acronyms regarding HRV indices and arterial pressure variables used in this manuscript can be seen in Table 1.

Previous research further suggests that endurance exercise training may alter HRV to reflect a more favorable cardiac autonomic balance (i.e. greater vagal modulation) in young, healthy individuals (Al-Ani, Munir, White, Townend, & Coote, 1996; De Meersman, 1992; Levy et al. 1998). For example, Al-Ani et al. reported that 6 weeks of cycling exercise at an intensity of 85% HR_{max} significantly elevated both HF and LF power. Furthermore, De Meersman reported that 8 weeks of running at an intensity of 75-90% HR_{max} significantly elevated the respiratory sinus arrhythmia, and Levy et al. reported significant elevations in the standard deviation of normal RR intervals following 6 months of training at 50-85% $HR_{reserve}$. Although the exact mechanism of this shift in sympathovagal balance has not yet been determined, there exists evidence of a reduction in right atrial beta-adrenergic receptor density (Hammond, White, Brunton, & Longhurst, 1987) and elevated acetylcholine concentration at the heart (De Schryver & Mertens-Strythagen, 1975). Furthermore, De Souza, Michelini, and

Table 1

Acronyms for HRV and Arterial Pressure Variables

Variable	**Definition**
Mean RR Interval (ms)	Average of all RR intervals over entire 5-min ECG recording
SDNN (ms)	Standard deviation of all RR intervals over entire 5-min ECG recording
TP (ms^2)	Total power; Power between 0.00 and 0.40 Hz of the heart rate power spectrum
LF (ms^2)	Low-frequency power; Power between 0.04 and 0.15 Hz of the heart rate power spectrum
HF (ms^2)	High-frequency power; Power between 0.15 and 0.40 Hz of the heart rate power spectrum
LFNU (%)	Low-frequency normalized units; LF/(LF+HF) * 100
HFNU (%)	High-frequency normalized units; HF/(LF+HF) * 100
ln	Natural logarithm
SBP (mmHg)	Systolic blood pressure
DBP (mmHg)	Diastolic blood pressure
MAP (mmHg)	Mean arterial pressure

Fior-Chadi (2001) recently reported a reduction in α_2-adrenoreceptor density and affinity in the rat medulla oblongata following exercise training.

Although it appears that endurance exercise training results in favorable alterations in autonomic control of the heart, the time course of these changes are not well understood. Most studies that have approached this issue have examined plasma catecholamine and/or heart rate at rest and during physical activity (Meredith et al. 1990; Mier, Turner, Ehsani, & Spina, 1997; Winder, Hagberg, Hickson, Ehsani, & McLane, 1978). For example, Winder et al. examined the time course of changes in plasma catecholamines in response to 40 minutes of interval training at 95% VO_{2max}, in a group of healthy males (age: 30±1 yr). They subsequently reported that heart rate, along with plasma norepinephrine (NE) and epinephrine (E) were reduced during submaximal exercise at the same absolute workload following six exercise sessions. Meredith et al. reported a significant reduction in resting heart rate and resting plasma NE following six 30-minute sessions of cycling at 60-70% VO_{2max}, with a further reduction following the ninth session. Additionally, Mier et al. reported a reduction in resting heart rate in healthy individuals (age: 26±2 yr) in response to 10 sessions of interval training on a cycle ergometer at 65-95% VO_{2peak}. However, the inferences that can be drawn from these studies are somewhat limited, mainly due to the inability of these techniques to clearly differentiate between the sympathetic and parasympathetic branches of the autonomic nervous system. Thus, it would be of interest to evaluate the time course of training-induced autonomic changes using HRV, which appears to be more sensitive to changes in sympathovagal balance (Pagani et al. 1986). Additionally, since altered indices of HRV have been associated with an increased risk of cardiac events (Tsuji at al. 1994), elucidation of a possible time course of any endurance training-induced alterations in HRV would be

clinically relevant in that it may provide clinicians with additional information regarding exercise programming in both healthy and at-risk populations.

Of concern when applying such a model is the observation that HRV appears to be influenced by acute laboratory conditions. For example, Hayano et al. (1994) reported that paced breathing results in a shift in the HRV power spectrum towards the HF range, a phenomenon thought to be a result of the respiratory sinus arrhythmia. Moreover, autonomic reactivity as observed under stressors such as head-up tilt may provide insight beyond that which is gleaned from resting measures alone. Furlan et al. (1993) reported that head-up tilt, which elicits a sympathetic outflow, results in a shift towards the LF range. At present it is not clear as to how HRV measured under different laboratory conditions might influence the sensitivity of HRV to detect training induced alterations in autonomic modulation of the heart.

Purposes

Therefore, the objectives of this investigation are to: 1) examine adaptations in cardiac autonomic modulation as measured by HRV under different conditions, including paced breathing and head-up tilt, in response to 8 endurance exercise training sessions performed over 2 weeks, and 2) to evaluate a possible time course of any training-induced alterations in autonomic modulation of the heart.

Hypotheses

It is hypothesized that participants undergoing 2 weeks of high-intensity exercise training will exhibit a greater relative vagal modulation of the heart, as identified by an increase in HF power, and a concurrent decrease in LF power, expressed as normalized units. Furthermore, in accordance with previous studies evaluating endurance training on markers of

autonomic activity, it is hypothesized that these training-induced alterations will be evident at least by the sixth training session.

Materials and Methods

Participants

Twenty-four participants (mean age = 23.1 years) were recruited from classes at Louisiana State University in Baton Rouge, and voluntarily completed all of the study requirements. Criteria for eligibility were: 1) male sex, 2) 18-30 years of age, 3) an energy expenditure of less than 2000 kcal•week^{-1} for the previous 3 months, and 4) a VO_{2peak} between 30-45 ml•kg^{-1}•min^{-1}. Exclusion criteria were: 1) presence of any documented cardiovascular, metabolic, or neurological disease, 2) regular consumption of any medication that influences the cardiovascular system, 3) participation in regular physical activity (an energy expenditure of greater than 2000 kcal•week^{-1}), and 4) a VO_{2peak} lower than 30 ml•kg^{-1}•min^{-1} or greater than 45 ml•kg^{-1}•min^{-1}.

Materials

The Health Status Questionnaire (Howley & Franks, 1997) was used to obtain details of each participant's health history and the Aerobics Center Longitudinal Study Physical Activity Questionnaire (Pereira et al. 1997) was used to evaluate the participants' level of habitual physical activity. A Biopac MP100 (Santa Barbara, CA) data acquisition system and AcqKnowledge ACK100 (Santa Barbara, CA) software program were used to capture, process, and analyze an electrocardiogram (ECG) signal. A SensorMedics Vmax 29c (Yorba Linda, CA) pulmonary gas exchange system was used for evaluation of each participant's peak oxygen consumption (VO_{2peak}) during a symptom-limited graded exercise test (SL-GXT) and a Monark 818E (Stockholm, Sweden) cycle ergometer was used for all exercise testing and training. Measures of arterial blood pressure during the SL-GXT and ECG collection were collected using a standard sphygmomanometer and stethoscope. Body composition was

evaluated using Lange skinfold calipers (Cambridge, MD). A standard physician's scale was used to evaluate participants' height and weight. All other information was obtained through a personal interview with each participant.

Procedure

Sequence of tests. On the initial visit to the laboratory, each participant gave written informed consent, completed the Health Status Questionnaire and physical activity questionnaire, was assessed for body composition, and completed a SL-GXT for determination of VO_{2peak}. Participants were then randomly assigned to either an exercise training group (EX) or to a control group (CT) via stratified random selection in an attempt to experimentally control for the possible influence of VO_{2peak} and physical activity on the dependent measures and treatment effects.

Following the initial assessment, the EX group underwent two-weeks of endurance exercise training, whereas the CT group was asked to maintain their previous level of physical activity. Training was performed four days per week (Monday, Tuesday, Thursday, and Friday). In order to evaluate the time course of any changes in HRV that occurred during the course of the training protocol, ECGs were collected and HRV was evaluated in both groups 2 times per week (Monday and Thursday) and at the same time of day as their previous ECG collection, with the EX group being evaluated prior to their exercise session. On the Monday immediately following the training period, all participants underwent a post-testing session, during which HRV, VO_{2peak}, and skinfold measures were reassessed, and the physical activity questionnaire was completed. The 5 days in which HRV was assessed were identified as Tests 1 through 5, respectively.

Assessment of peak oxygen consumption. A SensorMedics Vmax 29c pulmonary gas exchange system (Yorba Linda, CA) was used to evaluate the participant's VO_{2peak} during a SL-GXT on an 818E Monark cycle ergometer (Stockholm, Sweden). The SensorMedics system was calibrated prior to each participant reporting to the laboratory. Upon reporting to the laboratory, participants were given detailed instructions regarding the SL-GXT and the participant was prepared as follows: 1) a Polar (Woodbury, NY) heart rate monitor was secured around the participant's thoracic region, 2) a mouthpiece with a flow sensor was attached to the Vmax system and inserted into the participant's mouth to sample expired air, and 3) a sphygmomanometer was secured around the participant's upper left arm for evaluation of blood pressure. The participant was then asked to sit upright on the cycle ergometer while resting heart rate, blood pressure, and cardiorespiratory measures were recorded. Following a brief resting period on the cycle ergometer, the participant was asked to begin cycling at 70 rpm at a workload of 0.5 Kp. The workload on the ergometer was progressively increased by 0.5 Kp every 2 minutes. Heart rate and ratings of perceived exertion (RPE) using the Borg's scale (American College of Sports Medicine, 2000) were recorded every minute. Additionally, arterial blood pressure was recorded during every stage of the test. The participant was encouraged to continue cycling until he could no longer maintain a pace of 70 rpm, at which time the workload was reduced to 0.5 Kp while the participant continued to pedal slowly for 2-4 minutes. Other cardiorespiratory variables measured during the SL-GXT included oxygen consumption (VO_2) in both relative ($ml \bullet kg^{-1} \bullet min^{-1}$) and absolute ($l \bullet min^{-1}$) units, minute ventilation (V_E), respiratory frequency (RF), tidal volume (V_T), volume of expired carbon dioxide (VCO_2), and the respiratory quotient (RQ). Three of the following criteria had to be met to ensure that the participant put

forth a maximal effort: 1) failure of heart rate to increase with further increases in intensity, 2) plateau of oxygen uptake with increased workload, 3) RQ of > 1.15, and 4) an RPE >17.

Assessment of body composition. Body composition was assessed using Lange skinfold calipers (Cambridge, MD). Skinfold measures were taken at the following sites on each participant and reported in millimeters: 1) chest, 2) tricep, 3) abdominal, 4) suprailliac, 5) subscapular, 6) mid-axillary, and 7) thigh. The sum of the 7 skinfold sites were used to estimate percent body fat using previously established equations (American College of Sports Medicine, 2000).

Physical activity questionnaire. In order to evaluate the participants' level of habitual physical activity, all participants completed the Aerobics Center Longitudinal Study Physical Activity Questionnaire (Pereira et al. 1997) prior to, and following participation in the study. This questionnaire asked the participants questions about their physical activity patterns for the previous 3 months. Metabolic equivalent (MET) values were assigned to the various activities reported using established guidelines (American College of Sports Medicine, 2000), and energy expenditure was initially recorded in units of MET•min•week^{-1}. Energy expenditure was then converted to units of kilocalories•week^{-1}.

Exercise training. The 2 weeks of endurance exercise training consisted of 40 minutes of cycling on an 818E Monark cycle ergometer (Stockholm, Sweden). Each exercise bout consisted of a 5-minute "warm-up" period (cycling with no added resistance), followed by 30 minutes of cycling at a resistance that elicited a heart rate of 80-85% $HR_{reserve}$, and ended with a 5-minute "cool-down" period (cycling with no added resistance). Exercise intensity was closely monitored using a Polar heart rate monitor (Woodbury, NY).

Data Acquisition

All procedures were performed in a controlled laboratory setting (23-24 °C; ~760 torr). Upon reporting to the laboratory, the participant was asked to lie supine on a tilt table. Ag/AgCl electrodes were then arranged on the participant's anterior side in a standard 3-lead configuration and the electrodes were connected to the Biopac MP100 data acquisition system (Santa Barbara, CA). The AcqKnowledge ACK100 software program (Santa Barbara, CA) was used to collect a continuous ECG signal at 500 Hz. Following a 15-minute resting period, ECG data was collected during a 5-minute period of paced breathing at a frequency of 12 cycles per minute (PB), during a 5-minute period in which the participant breathed spontaneously (SB1), during a 5-minute period of 70-degree head-up tilt (TILT), and during a subsequent 5-minute period of supine rest (SB2). Arterial pressure was assessed at the midpoint of each 5-minute period.

Data Analysis

HRV was evaluated in accordance with guidelines previously set forth (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). ECGs were visually inspected for non-sinus beats and, if no ectopy was found, were subsequently plotted as a tachogram of heart period. The tachograms were then evaluated for the mean and standard deviation of all normal RR intervals (SDNN). Spectral analysis of HRV was derived via a 1024-point linear fast Fourier Transformation using a Hamming window. The resultant power density spectrum was then analyzed for total power (TP; 0.00-0.40 Hz), LF (0.04-0.15 Hz), and HF (0.15-0.40 Hz). LF and HF were further normalized (LFNU and HFNU) to better quantify sympathovagal balance. Systolic (SBP) and diastolic (DBP) arterial blood pressures were initially recorded and were used to

calculate mean arterial pressure (MAP) using the equation: MAP = DBP + 1/3 (SBP-DBP).

Statistical Analysis

All statistical analyses were performed with the SAS statistical package (Cary, NC). The Shapiro-Wilk test of normality was performed on all variables and those that violated assumptions of normality were transformed using the natural log (ln) algorithm. All tests were considered significant at the 0.05 level.

Descriptive and cardiorespiratory measures. Independent T-Tests were used to examine any initial group differences in age and height. A mixed-model, two-way analysis of variance (ANOVA) with repeated measures was used to examine main effects of group or training period, and group X training period interactions on body weight, body composition, or physical activity between groups. Similarly, a mixed-model, two-way ANOVA with repeated measures was used to examine cardiorespiratory measures at rest and at peak exercise during the SL-GXT. When a significant Group X Time interaction was found, a one-way repeated measures ANOVA was used to test for simple effects and identify any pre-post differences within each group.

Heart rate variability and arterial pressures during each testing session. HRV indices and arterial pressures collected each testing session (Test 1 through Test 5) were analyzed with a mixed model, two-way ANOVA with repeated measures to examine differences between groups and conditions. When a significant Group X Condition interaction was found, a one-way repeated measures ANOVA was used to test for simple effects, and thus identify any differences between conditions for each group. When the test for simple effects was significant, post-hoc contrasts were used to identify which conditions differed from each other. Similarly, when a significant main effect of Condition was found in the absence of a

Group X Condition interaction, contrasts were used to identify differences between conditions.

Heart rate variability and arterial pressures across time. HRV and arterial pressures collected during each condition (PB, SB1, TILT and SB2) were analyzed with a mixed model, two-way ANOVA with repeated measures to examine differences between groups and testing sessions. When a significant Group X Time interaction was found, a one-way repeated measures ANOVA was used to test for simple effects, and thus identify any differences between testing sessions for each group. When the test for simple effects was significant, post-hoc contrasts were used to identify which tests significantly differed from Test 1. Similarly, when a significant main effect of Time was found in the absence of a Group X Time interaction, contrasts were used to identify which tests significantly differed from Test 1.

Results

Descriptive Statistics

Descriptive statistics for the participants can be seen in Table 2. There were no between group differences in height or weight. Two-way ANOVA with repeated measures revealed a main effect of Time on percent body fat ($F[1,22] = 8.21$, $p<0.01$), indicating lower body fat for the entire group at post-test. Furthermore, analysis of the PAQ revealed a Group X Time interaction ($F[1,22] = 5474.37$, $p<0.01$) such that EX reported an increase in physical activity at the post-test.

Table 2

Descriptive Statistics for the Participants (Mean, sd)

Group	Age (yr)	Height (inches)	Weight (kg)		Body Fat (%)		PAQ (kcal•week^{-1})	
			Pre	Post	Pre	Post	Pre	Post
EX	23.13	69.62	82.616	82.216	18.16	17.26†	1685.8387	3795.0406†
CT	23.14	69.14	79.113	79.113	15.35	15.05†	1704.9428	1721.0419.6

PAQ = physical activity questionnaire
† = $p<0.05$ vs. pre

Cardiorespiratory Measures

Cardiorespiratory measures at rest and at peak exercise can be seen in Table 3. ANOVA revealed a main effect of Group on resting RQ ($F[1,22] = 4.42$, $p<0.05$), reflecting that CT had lower values of RQ. There was also a main effect of Time on resting VO_2 ($F[1,22] = 5.24$, $p<0.05$), V_E ($F[1,22] = 6.58$, $p<0.05$), RF ($F[1,22] = 4.37$, $p<0.05$), and V_T ($F[1,22] = 8.81$, $p<0.01$). These were such that VO_2, V_E, and V_T were greater and RF was lower during the post-test for both groups. ANOVA revealed Group X Time interactions on

Table 3

Cardiorespiratory Measures at Rest and at Peak Exercise (Mean, sd)

Group	VO_2 ($ml \bullet kg^{-1} \bullet min^{-1}$)		V_E ($l \bullet min^{-1}$)		RF ($breaths \bullet min^{-1}$)		V_T ($l \bullet breath^{-1}$)		RQ		HR ($beats \bullet min^{-1}$)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
EX (Rest)	4.62 1.1	5.36 1.4†	15.7 4.1	17.0 4.6†	20.6 4.9	17.9 3.4†	0.88 0.3	1.03 0.3††	1.04 0.1	1.07 0.1	83.1 12	83.3 14
CT (Rest)	5.60 1.8	6.44 2.1†	15.0 2.5	16.9 4.4†	18.8 3.9	18.2 5.1†	0.88 0.3	1.05 0.3††	0.98 0.1‡	0.99 0.1‡	73.5 15	75.7 14
EX (Peak)	33.48 3.7	36.07 3.2††	113.3 21	126.6 24†	41.2 8	43.7 8	2.83 0.7	2.98 0.7	1.33 0.1	1.35 0.1	184.4 10	185.3 10
CT (Peak)	33.88 3.0	32.65 2.6	113.6 24	108.5 17	41.4 8	39.8 8	2.82 0.6	2.66 0.6	1.34 0.1	1.31 0.1	181.2 10	178.9 8

VO_2 = oxygen consumption
V_E = minute ventilation
RF = respiratory frequency
† = $p<0.05$ vs. pre
†† = $p<0.01$ vs. pre
‡ = $p<0.05$ vs. EX
V_T = tidal volume
RQ = respiratory quotient
HR = heart rate

VO_{2peak} ($F[1,22] = 15.46$, $p<0.01$), V_{Epeak} ($F[1,22] = 11.66$, $p<0.01$), and V_{Tpeak} ($F[1,22] = 4.68$, $p<0.05$). These interactions were such that EX experienced increases in VO_{2peak} ($F[1,11] = 12.7$, $p<0.01$) and V_{Epeak} ($F[1,11] = 6.01$, $p<0.05$) across time, whereas these variables were unaltered in CT.

Heart Rate Variability and Arterial Blood Pressure Within the Testing Sessions

HRV values observed within each testing session are reported in Tables 4 through 8. ANOVA revealed a Group X Condition interaction on the mean RR interval only during Test 1 ($F[3,66] = 3.0$, $p<0.05$). Tests for simple effects revealed that there were changes in the mean RR interval over each condition in both CT ($F[3,33] = 102.2$, $p<0.01$) and EX ($F[3,33] = 25.08$, $p<0.01$). Contrasts found that in EX, the mean RR interval during TILT was less than that during the other three conditions ($p<0.01$), while in CT, the mean RR interval during each condition were all different from each other ($p<0.01$). During Tests 2 through 5 there were main effects of Condition on the mean RR interval ($p<0.01$). Contrasts revealed during these tests, the mean RR interval during TILT was lower than that during the other three conditions ($p<0.05$), and also that the mean RR interval during SB2 was greater than that during PB and SB1 ($p<0.05$). Additionally, during Test 2, the mean RR interval during SB1 was greater than that during PB ($p<0.05$).

ANOVA also revealed a main effect of Condition on SDNN that was consistent across all testing sessions. Post-hoc contrasts revealed that SDNN during TILT was significantly lower than that during the other three conditions during Tests 1 through 4 ($p<0.01$). Additionally within Test 2, SDNN during SB2 was higher than that during PB ($p<0.05$). Furthermore within Test 5, SDNN during TILT was significantly lower than that during PB and SB2 ($p<0.05$), and SDNN during SB2 was greater than that during SB1 ($p<0.05$).

Table 4

HRV During Test 1 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
Mean RR (ms)	925.88 137.3	948.3 140	759.7 108*	987.2 160	956.56 105.5†‡	1028.8 124‡	776.2 104*	1092.9 142
SDNN (ms)	74.3 32	72.5 33	64.4 31*	80.1 21	81.7 29	85.4 29	62.1 26*	90.3 19
lnLFNU (ln%)	3.45 0.5†‡	4.07 0.2‡	4.42 0.2*	3.79 0.3	3.43 0.4†‡	3.88 0.4‡	4.39 0.2*	3.68 0.5
lnHFNU (ln%)	4.17 0.2†‡	3.61 0.5‡	2.53 0.7*	3.93 0.4	4.16 0.3†‡	3.77 0.5‡	2.69 0.7*	3.96 0.4
lnLF/ lnHF	0.90 0.1†‡	1.08 0.1‡	1.46 0.3*	0.99 0.1	0.90 0.1†‡	1.03 0.1‡	1.40 0.2*	0.96 0.1

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
TP = total power
LF = low-frequency power
NU = normalized units
ms = milliseconds
* = $p<0.05$ vs. other 3 conditions for specified group
† = $p<0.05$ vs. SB1 for specified group
‡ = $p<0.05$ vs. SB2 for specified group

Table 5

HRV During Test 2 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
Mean RR (ms)	923.64 112.6†‡	951.8 115‡	736.0 83*	1009.0 107	969.42 102.5†‡	1051.3 138‡	787.0 131*	1090.2 142
SDNN (ms)	77.0 38‡	77.5 36	63.5 28*	95.4 32	84.3 29‡	89.3 28	60.7 25*	88.9 14
lnLFNU (ln%)	3.29 0.7†‡	4.06 0.2	4.40 0.1*	3.94 0.4	3.19 0.5†‡	3.92 0.4	4.39 0.2*	3.75 0.4
lnHFNU (ln%)	4.17 0.3†‡	3.66 0.3	2.78 0.5*	3.73 0.4	4.28 0.2†‡	3.75 0.5	2.71 0.6*	3.94 0.4
lnLF/ lnHF	0.89 0.1†‡	1.07 0.1	1.40 0.2*	1.05 0.1	0.85 0.1†‡	1.03 0.1	1.44 0.3*	0.98 0.1

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
TP = total power
LF = low-frequency power
NU = normalized units
ms = milliseconds
* = $p<0.05$ vs. other 3 conditions for specified group
† = $p<0.05$ vs. SB1 for specified group
‡ = $p<0.05$ vs. SB2 for specified group

Table 6

HRV During Test 3 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
Mean RR (ms)	958.3 101‡	971.8 145‡	768.2 137*	1036.2 165	998.23 97.2‡	1053.5 100‡	797.7 130*	1123.5 98
SDNN (ms)	91.0 50	78.4 30	69.4 21*	94.4 31	82.9 32	83.4 35	63.8 26*	84.7 31
lnLFNU (ln%)	3.36 0.7†‡	3.99 0.3	4.39 0.2*	3.83 0.3	3.26 0.5†‡	3.83 0.4	4.46 0.1*	3.73 0.4
lnHFNU (ln%)	4.14 0.3†‡	3.70 0.5	2.75 0.6*	3.89 0.4	4.25 0.2†‡	3.84 0.5	2.36 0.8*	3.95 0.6
lnLF/ lnHF	0.91 0.1†	1.07 0.2	1.38 0.2*	1.00 0.1	0.86 0.1	0.99 0.1	1.54 0.3*	0.97 0.1

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
TP = total power
LF = low-frequency power
NU = normalized units
ms = milliseconds
* = $p<0.05$ vs. other 3 conditions for specified group
† = $p<0.05$ vs. SB1 for specified group
‡ = $p<0.05$ vs. SB2 for specified group

Table 7

HRV During Test 4 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
Mean RR (ms)	958.33 123‡	982.9 155‡	775.4 126*	1039.5 166	965.22 161‡	1004.7 156‡	773.6 131*	1091.5 145
SDNN (ms)	91.8 52	85.9 30	71.6 30*	89.8 25	79.4 32	87.5 33	61.3 26*	90.6 25
lnLFNU (ln%)	3.31 0.8†‡	4.07 0.3	4.41 0.2*	3.89 0.4	3.19 0.6†‡	3.88 0.5	4.40 0.1*	3.82 0.4
lnHFNU (ln%)	4.09 0.4†‡	3.56 0.5	2.62 0.7*	3.75 0.5	4.24 0.2†‡	3.79 0.4	2.72 0.6*	3.81 0.6
lnLF/ lnHF	0.91 0.2†‡	1.11 0.2	1.48 0.4*	1.04 0.2	0.85 0.1†‡	1.02 0.1	1.42 0.3*	1.01 0.2

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
TP = total power
LF = low-frequency power
NU = normalized units
ms = milliseconds
* = $p<0.05$ vs. other 3 conditions for specified group
† = $p<0.05$ vs. SB1 for specified group
‡ = $p<0.05$ vs. SB2 for specified group

Table 8

HRV During Test 5 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
Mean RR (ms)	985.34 149‡	983.2 167‡	773.2 142*	1025.0 185	987.06 100‡	1042.2 140‡	801.7 108*	1116.0 159
SDNN (ms)	99.3 56	79.8 32‡	79.7 50‡ϕ	101.2 30	91.1 29	87.8 23‡	68.0 29‡ϕ	93.5 27
lnLFNU (ln%)	2.89 0.8*	4.06 0.3	4.12 0.2	3.63 0.4	3.36 0.5†	3.84 0.5	4.41 0.1*	3.67 0.3
lnHFNU (ln%)	4.32 0.2	3.59 0.44ϕ	3.52 0.5ϕ	4.01 0.4	4.19 0.2	3.78 0.5	2.65 0.6*	4.03 0.3
lnLF/ lnHF	0.82 0.1	1.10 0.1‡ϕ	1.12 0.1‡ϕ	0.96 0.1ϕ	0.89 0.1	1.01 0.1	1.41 0.2*	0.95 0.1

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
TP = total power
LF = low-frequency power
NU = normalized units
* = $p<0.05$ vs. other 3 conditions for specified group
† = $p<0.05$ vs. SB1 for specified group
‡ = $p<0.05$ vs. SB2 for specified group
ϕ = $p<0.05$ vs. PB

Regarding the spectral indices, there were main effects of Condition on lnLFNU and lnHFNU during Tests 1 through 4. Contrasts then revealed that lnLFNU was greater (and lnHFNU was lower) during TILT compared to the other three conditions ($p<0.05$), and that lnLFNU was lower (and lnHFNU was greater) during PB compared to SB1 and SB2 ($p<0.05$). Likewise, there was also a main effect of Condition on lnLF/lnHF during Tests 1, 2, and 4 ($p<0.01$). Contrasts revealed that during these tests, lnLF/lnHF during TILT was greater than that during the other three conditions ($p<0.05$), and that lnLF/lnHF during PB was less than that during SB1 and SB2 ($p<0.05$). Exclusively during Test 5, there were Group X Condition interactions on lnLFNU ($F[3,66] = 3.33$, $p<0.01$), lnHFNU ($F[3,66] = 8.81$, $p<0.01$), and lnLF/lnHF ($F[3,66] = 10.39$, $p<0.01$). Tests for simple effects found that both EX and CT displayed differences in lnLFNU, lnHFNU, and lnLF/lnHF between the conditions ($p<0.01$). Contrasts revealed that lnLFNU during PB was significantly lower than the other three conditions in EX ($p<0.05$), whereas in CT, lnLFNU during TILT was greater than that during the other three conditions ($p<0.05$) and lnLFNU during PB was less than that during SB1 and TILT ($p<0.05$). Additionally, contrasts found that lnHFNU during PB was greater than that during SB1 and TILT in EX ($p<0.05$), whereas in CT, lnHFNU during TILT was lower than that during the other three conditions ($p<0.05$). Contrasts also revealed that while lnLF/lnHF during TILT was greater than that during the other three conditions in CT ($p<0.05$), in EX lnLF/lnHF during PB was lower than the other three conditions ($p<0.05$), and lnLF/lnHF during SB2 was lower than SB1 and TILT ($p<0.05$). Lastly, during Test 3 there was a Group X Condition interaction on lnLF/lnHF ($p<0.05$). Tests for simple effects found that both CT ($p<0.01$) and EX ($p<0.01$) exhibited changes in lnLF/lnHF across time. Contrasts revealed that lnLF/lnHF during TILT was greater than that of the other three

conditions in CT ($p<0.05$), while in EX, lnLF/lnHF was lower during PB compared to SB1 ($p<0.05$) in addition to lnLF/lnHF during TILT being greater than the other three conditions ($p<0.05$).

Arterial blood pressures within Tests 1 through 5 can be seen in Tables 9 though 13, respectively. ANOVA revealed a main effect of Condition on DBP and MAP within all Tests ($p<0.01$). Post-hoc contrasts revealed that DBP and MAP were higher during TILT compared to the other three conditions ($p<0.01$). Additionally, DBP and MAP were greater during PB compared to SB2 during Test 3 ($p<0.05$), and greater during PB compared to SB1 during Test 4 ($p<0.05$). There was also a main effect of Condition on SBP within Tests 2 and 5 ($p<0.05$). Contrasts revealed that during Test 2, SBP was lower during TILT compared to the other three conditions ($p<0.01$), and further that during Test 5, SBP was lower during TILT compared to SB2 ($p<0.05$).

Table 9

Blood Pressure Responses During Test 1 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
SBP (mmHg)	118.2 11	117.3 11	116.8 11	118.3 10	117.3 12	115.3 12	113.5 12	115.0 14
DBP (mmHg)	76.5 6	76.8 8	87.8 6*	76.7 6.9	74.0 6	73.0 7.6	84.8 8*	74.2 7
MAP (mmHg)	90.4 6	90.3 8	97.5 7*	90.5 6	88.4 6	87.1 5	94.4 8*	87.8 6

SBP = systolic blood pressure * = $p<0.05$ vs. other 3 conditions for specified group
DBP = diastolic blood pressure
MAP = mean arterial pressure

Table 10

Blood Pressure Responses During Test 2 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
SBP (mmHg)	116.6 8	117.7 5	112.2 6*	116.8 10	115.7 13	113.8 10	108.7 12*	113.0 13
DBP (mmHg)	76.2 7	77.0 6	88.3 8*	74.5 7	73.7 8	71.8 6	85.8 8*	72.7 8
MAP (mmHg)	89.7 7	90.5 5	96.3 7*	88.6 8	87.7 8	85.8 6	93.4 9*	86.1 8

SBP = systolic blood pressure * = $p<0.05$ vs. other 3 conditions for specified group
DBP = diastolic blood pressure
MAP = mean arterial pressure

Table 11

Blood Pressure Responses During Test 3 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
SBP (mmHg)	116.3 10	116.8 11	116.2 11	114.7 11	112.8 11	112.0 12	110.3 12	112.2 12
DBP (mmHg)	75.3 9‡	72.8 8	87.5 7*	71.8 6	73.2 7‡	73.2 6	84.0 7*	71.8 5
MAP (mmHg)	89.0 8‡	87.5 9	97.0 7*	86.1 7	86.4 7‡	86.1 8	92.8 8*	85.3 7

SBP = systolic blood pressure * = $p<0.05$ vs. other 3 conditions for specified group
DBP = diastolic blood pressure ‡ = $p<0.05$ vs. SB2 for specified group
MAP = mean arterial pressure

Table 12

Blood Pressure Responses During Test 4 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
SBP (mmHg)	115.8 13	112.7 13	114.0 10	113.8 11	111.5 9	111.3 13	111.0 12	115.0 13
DBP (mmHg)	75.3 9†	74.2 8	86.8 10*	74.5 8	75.2 6†	72.8 6	85.8 6*	72.7 7
MAP (mmHg)	88.8 10†	87.0 9	95.9 9*	87.6 8	87.3 6†	85.7 7	94.2 6*	86.8 6

SBP = systolic blood pressure
DBP = diastolic blood pressure
MAP = mean arterial pressure
* = $p<0.05$ vs. other 3 conditions for specified group
† = $p<0.05$ vs. SB1 for specified group

Table 13

Blood Pressure Responses During Test 5 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
SBP (mmHg)	120.8 10	120.8 12	116.3 13‡	119.5 10	112.3 10	111.8 12	110.0 11‡	113.8 12
DBP (mmHg)	74.8 7	75.3 8	87.3 8*	75.7 5	73.3 6	72.5 6	85.7 7*	72.5 5
MAP (mmHg)	90.2 7	90.5 8	97.0 9*	90.3 6	86.3 6	85.6 6	93.8 8*	86.2 6

SBP = systolic blood pressure
DBP = diastolic blood pressure
MAP = mean arterial pressure
* = $p<0.05$ vs. other 3 conditions for specified group
‡ = $p<0.05$ vs. SB2 for specified group

Heart Rate Variability and Arterial Blood Pressure Across Time

Paced breathing. ANOVA revealed a main effect of Time ($p<0.01$) on SDNN. Contrasts revealed that SDNN during Test 5 was greater than during Test 1 ($p<0.01$). Regarding the spectral indices, there were Group X Time interactions on lnLFNU ($p<0.05$) (Figure 1) and lnLF/lnHF ($p<0.05$) (Figure 2). Tests for simple effects found that these variables were not altered across time in CT, whereas lnLFNU and lnLF/lnHF were lower during Test 5 compared to Test 1 ($p<0.01$) in EX. The Group X Time interaction for lnHFNU, however, fell short of statistical significance ($F[4,88] = 2.36$, $p=0.06$), as did the main effects of Group and Time. Furthermore, there were no main effects of Group or Time, nor were there any Group X Time interactions on arterial blood pressure.

Spontaneous breathing. There were no main effects of Group or Time, nor Group X Time interactions on the mean RR interval, HRV parameters, or arterial blood pressure during SB1. During SB2, ANOVA revealed a main effect of Time on lnLF/lnHF ($p<0.05$). However, contrasts revealed that there were no differences in lnLF/lnHF between Test 1 and any of the other tests. Additionally, there were no main effects of Group or Time, nor Group X Time interactions on arterial blood pressure during SB2.

Head-up tilt. ANOVA revealed Group X Time interactions on lnLFNU ($p<0.01$) (Figure 1), lnHFNU ($p<0.01$), and lnLF/lnHF ($p<0.05$) (Figure 2). Tests for simple effects revealed no change in spectral parameters for CT, but that EX displayed greater lnHFNU ($p<0.01$), and lower lnLFNU ($p<0.01$) and lnLF/lnHF ($p<0.01$) during Test 5 compared to Test 1. Additionally, there were no main effects of Group or Time, nor Group X Time interactions on arterial blood pressure.

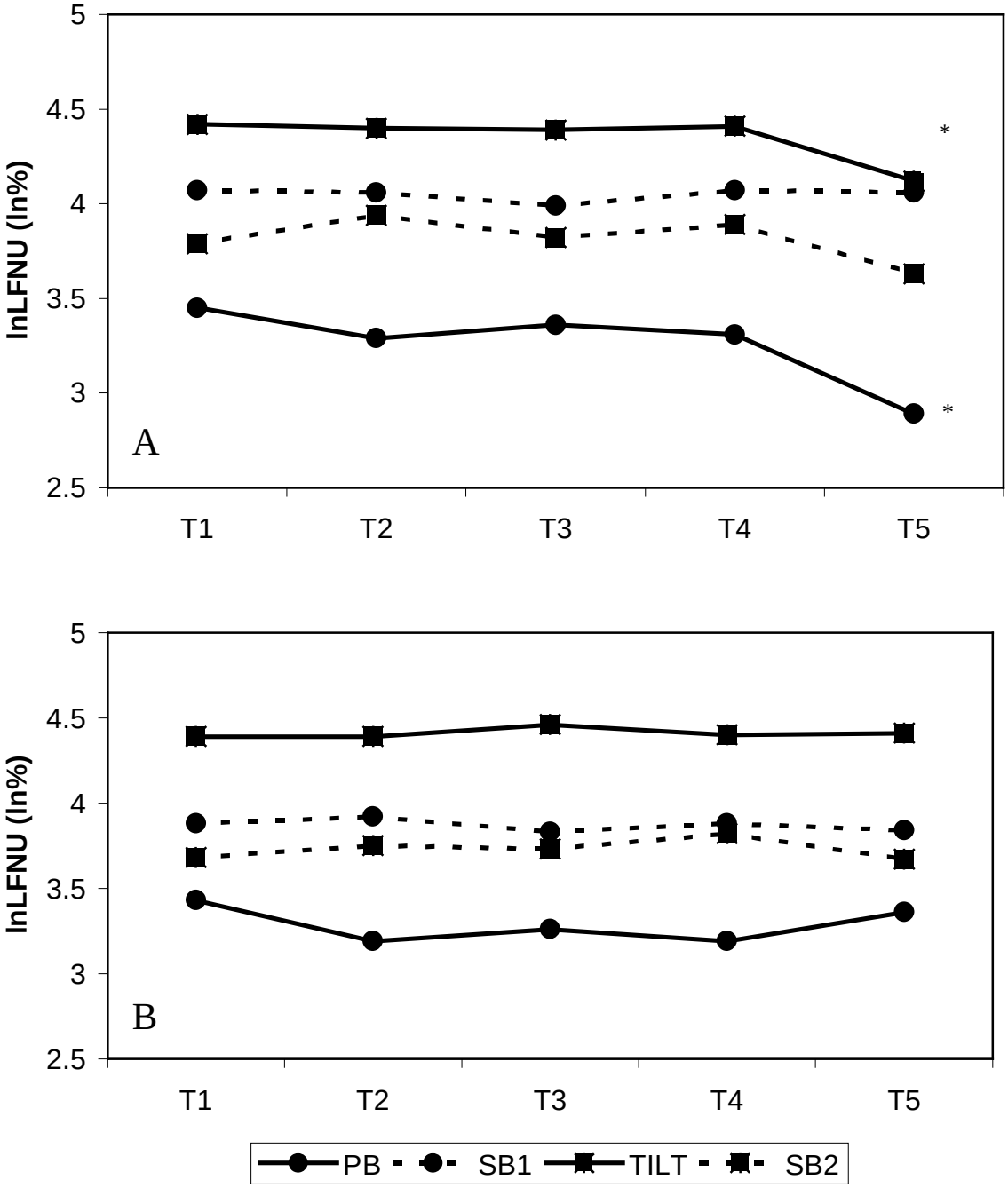

Figure 1 LnLFNU During the 4 Conditions Across Time in A) EX and B) CT

* = $p<0.05$ vs. T1 for specified group

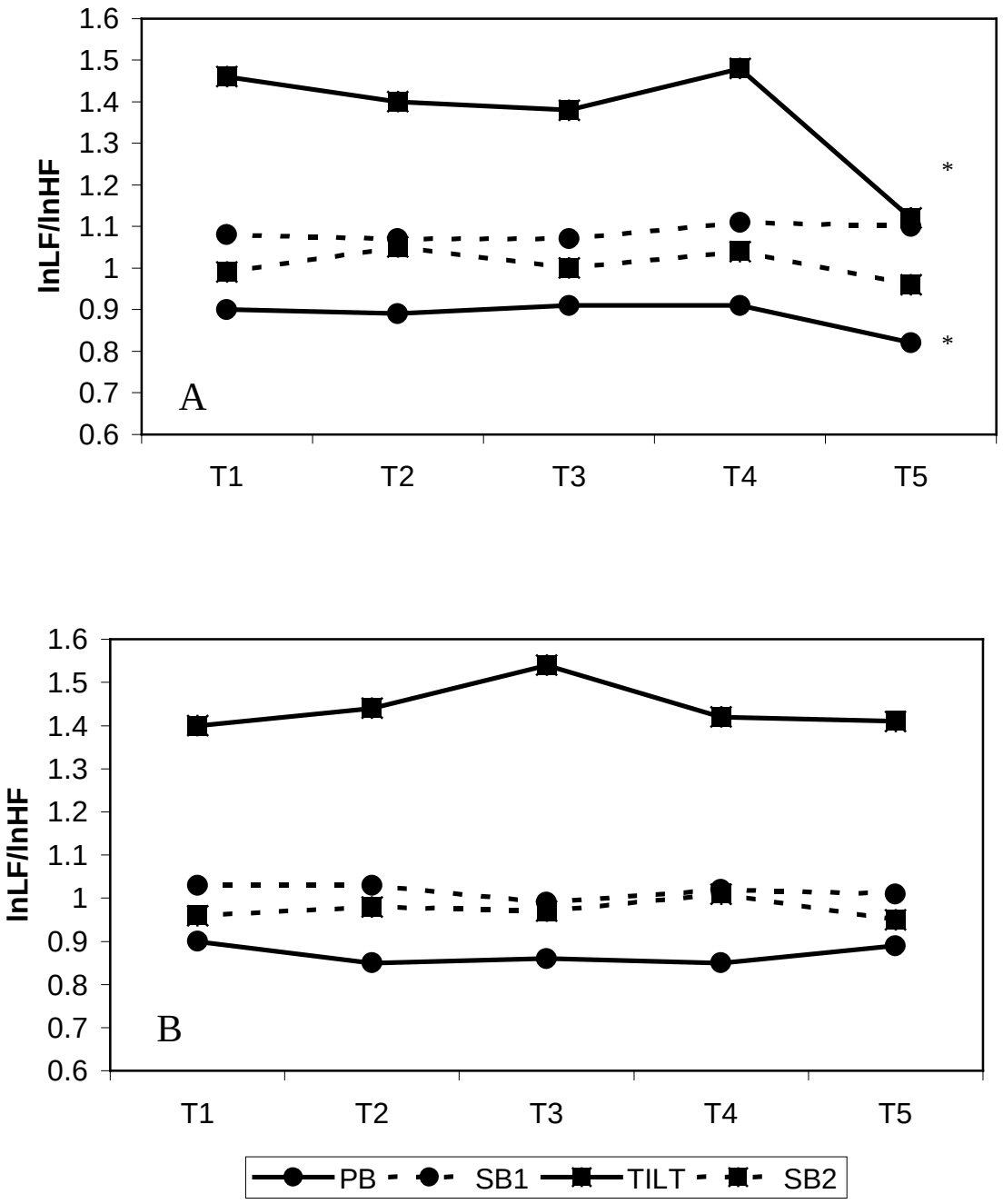

Figure 2 LnLF/lnHF During the 4 Conditions Across Time in A) EX and B) CT

* = $p<0.05$ vs. T1 for specified group

Discussion

This investigation examined the influence of 2 weeks of exercise training, 4 days per week, 40 minutes per session, at 80-85% $HR_{reserve}$, on cardiorespiratory fitness and vagal modulation of the heart. The initial values obtained for the cardiorespiratory variables and HRV are consistent with other studies using participants of similar fitness levels (Furlan et al. 1993; Mier et al. 1997). For example, the initial range of VO_{2peak} of our participants (30 to 41 $ml \bullet kg^{-1} \bullet min^{-1}$) is nearly identical to that of Mier et al., and the mean values of RR intervals (940 ms), SDNN (77.5 ms), and normalized power (lnLFNU: 3.4 & lnHFNU: 4.2) are in line with Furlan et al. With respect to the influence of training, participants in the treatment group improved their cardiorespiratory fitness, as indicated by an 8% increase in VO_{2peak} from 33.5 to 36.1 $ml \bullet kg^{-1} \bullet min^{-1}$, whereas the control group exhibited no such changes in this parameter. A training effect of this magnitude appears to be consistent with the 10% improvement in VO_{2peak} reported by Mier et al. in response to 10 days of training.

HRV was examined under a variety of conditions, both to examine its construct validity, as well as to examine the extent to which these conditions expose alterations in autonomic behavior following periods of exercise training. Of particular interest was the influence that breathing pattern might have on autonomic modulation of the heart. Therefore, paced and spontaneous breathing conditions were included. In addition, the autonomic adjustment to head-up tilt was of interest inasmuch as autonomic reactivity may provide information that is unique from resting autonomic modulation alone. To this end, there were some general observations regarding the influences of the different conditions on HRV.

With respect to the influence of breathing pattern, the present data revealed that lnLFNU and lnLF/lnHF were lower and lnHFNU was greater during PB compared to the

other conditions, including SB. These findings are consistent with previous reports that PB results in an elevation of power in the HF range of the power spectrum (Hayano et al. 1994). This phenomenon is thought to be a result of an augmented respiratory sinus arrhythmia due to input from pulmonary stretch receptors and/or modulation of cardiomotor neurons in the central respiratory center (Hayano et al.).

With respect to the orthostatic challenge, TILT resulted in a significant reduction of the mean RR interval (i.e. increase in heart rate). Moreover, this was typically accompanied by increases in lnLFNU and lnLF/lnHF and decreases in SDNN and lnHFNU with the exception of Test 5. These findings are consistent with previous reports that TILT results in a greater sympathetic outflow and/or a vagal withdrawal (Furlan et al. 1993). Furthermore, 5 minutes of TILT resulted in a consistent elevation of DBP and MAP. This response, which was observed on each test day, is further evidence of an increased sympathetic outflow following 5 minutes of TILT. Such a response appears to be mediated by the baroreflex mechanism.

The behavior of HRV and hemodynamics described above are consistent with our understanding of cardiovascular regulation during such laboratory conditions, and therefore the results suggest some degree of construct validity. The primary purpose of this investigation, however, was to examine the response of these parameters to 8 exercise training sessions performed over 2 weeks. Previous studies have demonstrated that endurance exercise training in young, healthy participants results in significant alterations in HRV that reflect an increased vagal modulation of the heart. For example, Al-Ani et al. (1996) reported that 6 weeks of cycling significantly elevates HF power. Furthermore, De Meersman (1992) and Levy et al. (1998) reported improvements in time domain indices of HRV following 8

weeks and 6 months of training, respectively. However, there is limited information regarding the time course of these training-induced changes. Thus, it was our intention to examine if 2 weeks of training could elicit such changes, and if so, to examine the time course of these alterations. The data from this investigation demonstrate that 8 sessions of high-intensity exercise training performed over 2 weeks is sufficient to alter HRV, but only as detected during the PB and head-up TILT conditions. Training effects were not observed during SB. During PB we found significant Group X Time interactions on lnLFNU and lnLF/lnHF. Further analysis revealed that both of these variables were lower (16 and 9%, respectively) during Test 5 compared to Test 1 in EX, while there were no differences across time in CT. These findings suggest that our training protocol resulted in a shift in sympathovagal balance favoring a greater relative vagal modulation of the heart. Although the Group X Time interaction did not reach statistical significance for SDNN and lnHFNU during PB, there was a trend towards an interaction for each of these indices ($p=0.08$ and $p=0.06$, respectively). Therefore, measures of HRV during the paced breathing condition are generally in agreement with previous work indicating a shift in sympathovagal balance following exercise training, and moreover suggest that this effect may not be observed until 8 training sessions into the training period.

During TILT, there were significant Group X Time interactions on lnLFNU, lnHFNU, and lnLF/lnHF. Specifically, the group undergoing exercise training displayed lower lnLFNU and lnLF/lnHF, and greater lnHFNU during Test 5 compared to Test 1, while CT exhibited no differences in these indices across time. Thus, an additional finding of this investigation is that 2 weeks of endurance exercise training may elevate the parasympathetic and/or lessen the sympathetic response to TILT. In further support of this hypothesis, during Test 5 there were

significant Group X Condition interactions on lnLFNU, lnHFNU, and lnLF/lnHF. These interactions were such that EX did not demonstrate the elevation of lnLFNU and lnLF/lnHF, or the reduction in lnHFNU during TILT that were present during the first 4 tests.

An unexpected finding of this investigation was that the mean RR interval, and thus heart rate, was not altered during any of the conditions following the training protocol. This was somewhat perplexing in that we detected alterations in HRV that indicate a reduction in sympathovagal balance, and also that a reduced resting heart rate is an established adaptation to exercise training (Wilmore et al. 2001). Possible explanations for this discrepancy include: 1) our assessment of the mean RR interval during conditions which the participants were not truly at rest, and 2) the possibility that the exercise training protocol used was insufficient to alter resting heart rate. However, it should be noted that although non-significant, the mean RR interval of the training group increased from 925 to 985 ms from Test 1 to Test 5, reflecting a reduction in heart rate from 65 to 61 beats per minute, during PB.

Our ability to detect a training effect on HRV only during PB and TILT suggests that HRV may be a more sensitive measure of training-induced changes in autonomic modulation when collected under such conditions. In fact, a few studies that have reported training-induced changes in HRV used a paced breathing protocol and/or head-up tilt (De Meersman, 1992; Hedelin, Bjerle, & Henriksson-Larson, 2001; Yamamoto, Miyachi, Saitoh, Yoshioka, & Onodera, 2001). The absence of any significant findings during SB further emphasizes the need for careful standardization procedures during collection of HRV data. Thus, the addition of either of these two conditions would be useful to any longitudinal investigation examining cardiac autonomic modulation.

The findings of the present investigation are somewhat consistent with Hedelin et al. (2001) who recently reported alterations in HRV following a 7-month training period in a group of canoeists and cross-country skiers. Following training, they reported a reduction in LF power during head-up tilt, and further that this reduction was significantly correlated with the change in VO_{2peak}. Although the participants in this study appear to have had higher fitness levels than our participants, the present findings are very similar. In contrast to the present study, however, Yamamoto et al. (2001) recently evaluated HRV following one week, 4 weeks, and 6 weeks of exercise training. They subsequently reported a significant increase in HF power after one-week of training, followed by no further increases over the rest of the training period. Whereas, we did not report any changes in autonomic modulation until the second week of training. This finding is perplexing, in that the training protocol of Yamamoto et al. was very similar to the present study (frequency: 4 days per week; duration: 40 minutes; intensity: 80% VO_{2peak}). However, Yamamoto gave no information regarding the participant's habitual level of physical activity and their participants had an initial fitness level that surpassed those of our participants (VO_{2peak} = 48.2 $ml \bullet kg^{-1} \bullet min^{-1}$). Loimaala, Huikuri, Oja, Pasanen, and Vuori (2000) reported no significant changes in HRV following a 5-month jogging protocol (frequency: 4-6 times/week; duration: 30 minutes; intensity: 75% of VO_{2max}). Possible reasons for the discrepancy between these results and our findings include: 1) the lower exercise intensity used compared to our study, 2) the lack of a paced breathing protocol during collection of HRV, and 3) the lack of daily supervision by Loimaala et al. This group only provided supervision during one exercise session a week, thus the researchers cannot be certain that the participants fully adhered to the training protocol.

Lastly, there are studies that have found changes suggesting heightened sympathetic activity following exercise training. Pichot et al. (2000) reported that during a 3-week high-intensity training protocol, there was a shift towards cardiac sympathetic dominance, marked by a loss of global HRV. At first glance, such findings might seem directly opposed to those of the present investigation. However, the participants in Pichot's study engaged in 6-10 exercise sessions a week, and therefore there may have been insufficient recovery between sessions, at least in terms of identifying a training adaptation on autonomic activity. This is somewhat supported by their data indicating that following a fourth "recovery" week, there was a shift back towards parasympathetic dominance, leading the authors to indicate that indeed there is an important aspect of a sufficient recovery period on autonomic modulation. Similarly, Furlan et al. (1993) reported an increase in cardiac sympathetic outflow, as identified by elevated LF power, following an acute bout of exercise that persists up to 24 hours following cessation of exercise. They further reported that this sympathetic elevation was absent 48 hours after the exercise bout. Inasmuch as the present investigation allowed at least 48 hours following the participant's last exercise session prior to collection of HRV data, thereby optimizing the recovery period, the findings of the present study stand in agreement with Pichot et al. and Furlan et al.

Thus, our finding of a training-induced reduction in sympathovagal balance is in general agreement with other research. While the present investigation cannot offer an explanation as to where training adaptations may occur, the appearance of training effects under some conditions, but not all, seems to suggest that the training adaptations extend beyond changes at the end-organ, alone. Otherwise it could be argued that pre vs. post training differences should have existed under any of the laboratory conditions (including

spontaneous breathing). One possible mechanism for our findings is an increased blood volume, which has been documented as an early adaptation to exercise training (Yang, Mack, Wolfe & Nadel, 1998). Spinelli et al. (1999) recently reported that acute plasma volume expansion via saline infusion resulted in an increase in the HF range of the HRV power spectrum. They subsequently suggested that increases in plasma volume activate arterial and cardiopulmonary baroreceptors, which inhibit sympathetic, and increase parasympathetic outflow from the cardiorespiratory center in the medulla. This could further explain how our participants were able to maintain arterial pressure during TILT with a lower sympathetic outflow following training. Other possible mechanisms include changes in receptor sensitivity at the cardiorespiratory center (De Souza et al. 2001) or adaptations in sensory organelles (e.g. baroreceptors) and afferent nerve traffic (Hedelin et al. 2001), or both.

In conclusion, our data suggest that 8 endurance exercise training sessions performed over 2 weeks significantly alters cardiac vagal modulation. We reported changes in HRV during PB and TILT that are consistent with a shift towards greater parasympathetic and/or lesser sympathetic modulation of the heart following training. Furthermore, these data suggest that it takes at least eight exercise training sessions to alter HRV. Our ability to only detect changes in autonomic modulation during PB and TILT suggests that either or both of these conditions should be included in any longitudinal investigation examining autonomic modulation of the heart. Lastly, in light of the fact that HRV provides a good indication of the likelihood of developing dangerous cardiac arrhythmias, these findings may have important implications regarding exercise prescription in both healthy and at-risk populations.

Summary

The results of this investigation suggest that 8 endurance exercise training sessions performed over 2 weeks significantly alters cardiac autonomic modulation. We reported a shift in sympathovagal balance favoring a vagal modulation of the heart following training. These changes were reflected by alterations in the HRV power spectrum such that there were increases in lnHFNU and decreases in lnLFNU. These alterations were only present during periods of paced breathing and head-up tilt. The changes in autonomic modulation during head-up tilt further suggest that 2 weeks of exercise training may attenuate the sympathetic outflow and/or the vagal withdrawal associated with an orthostatic challenge. An additional finding of this study was that these training-induced alterations in cardiac autonomic modulation are not evident until the eighth training session. Our ability to detect these changes in cardiac autonomic modulation only during periods of paced breathing and head-up tilt suggests that these conditions should be included in any longitudinal investigation examining autonomic modulation of the heart. Lastly, given the close association between HRV indices and risk of unfavorable cardiac events, these findings may have implications regarding exercise programming in both healthy and at-risk populations.

References

Akselrod, S., Gordon, D., Ubel, F. A., Shannon, D. C., Barger, A. C., & Cohen, R. J. (1981). Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control. Science, 213, 220-222.

Al-Ani, M., Munir, S. M., White, M., Townend, J., & Coote, J. H. (1996). Changes in R-R variability before and after endurance training measured by power spectral analysis and by the effect of isometric muscle contraction. European Journal of Applied Physiology, 74, 397-403.

American College of Sports Medicine. (2000). ACSM's Guidelines for Exercise Testing and Prescription (6^{th} ed.). Philadelphia: Lippincott, Williams, and Wilkins.

Berntson, G. G., Bigger, J. T., Eckberg, D. L., Grossman, P., Kaufmann, P. G., Malik, M., Nagaraja, H. N., Porges, S. W., Saul, J. P., Stone, P. H., & van der Molen, M. W. (1997). Heart rate variability: origins, methods, and interpretive caveats. Psychophysiology, 34, 623-648.

De Meersman, R. E. (1992). Respiratory sinus arrhythmia alteration following training in endurance athletes. European Journal of Applied Physiology, 64, 434-436.

De Schryver, C., & Mertens-Strythagen, J. (1975). Heart tissue acetylcholine in chronically exercised rats. Experientia, 31, 316-318.

De Souza, C. G. G. T., Michelini, L. C., & Fior-Chadi, D. R. (2001). Receptor changes in the nucleus tractus solitarii of the rat after exercise training. Medicine and Science in Sports and Exercise, 33, 1471-1476.

Furlan, R., Piazza, S., Dell'Orto, S., Gentile, E., Cerutti, S., Pagani, M., & Malliani, A. (1993). Early and late effects of exercise and athletic training on neural mechanisms controlling heart rate. Cardiovascular Research, 27, 482-488.

Hammond, H. K., White, F. C., Brunton, L. L., & Longhurst, J. C. (1987). Association of decreased myocardial beta-receptors and chronotropic response to isoproterenol and exercise in pigs following chronic dynamic exercise. Circulation Research, 60, 720-726.

Hayano, J., Mukai, S., Sakakibara, M., Okada, A., Takata, K., & Fujinami, T. (1994). Effects of respiratory interval on vagal modulation of heart rate. American Journal of Physiology, 267, H33-H40.

Hedelin, R., Bjerle, P., & Henriksson-Larson, K. (2001). Heart rate variability in athletes: relationship with central and peripheral performance. Medicine and Science in Sports and Exercise, 33, 1394-1398.

Howley, E., & Franks, B. (1997). Health Fitness Instructor's Handbook (3^{rd} ed.). Champaign: Human Kinetics.

Levy, W. C., Cerqueira, M. D., Harp, G. D., Johannessen, K., Abrass, I. B., Schwartz, R. S., & Stratton, J. R. (1998). Effect of endurance exercise training on heart rate variability at rest in healthy young and older men. The American Journal of Cardiology, 82, 1236-1241.

Loimaala, A., Huikuri, H., Oja, P., Pasanen, M., & Vuori, I. (2000). Controlled 5-mo aerobic training improves heart rate but not heart rate variability or baroreflex sensitivity. Journal of Applied Physiology, 89, 1825-1829.

Meredith, I. T., Jennings, G. L., Esler, M. D., Dewar, E. M., Bruce, A. M., Fazio, V. A., & Korner, P. I. (1990). Time-course of the antihypertensive and autonomic effects of regular endurance exercise in human subjects. Journal of Hypertension, 8, 859-866.

Mier, C. M., Turner, M. J., Ehsani, A. A., & Spina, R. J. (1997). Cardiovascular adaptations to 10 days of cycle exercise. Journal of Applied Physiology, 83, 1900-1906.

Pagani, M., Lombardi, F., Guzzetti, S., Rimoldi, O., Furlan, R., Pizzinelli, P., Sandrone, G., Malfatto, G., Dell'Orto, S., Piccaluga, E., Turiel, M., Baselli, G., Cerutti, S., & Malliani, A. (1986). Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog. Circulation Research, 59, 178-193.

Pereira, M. A., Fitzgerald, S. J., Gregg, E. W., Joswiak, M. L., Ryan, W. J., Suminski, R. R., Utter, A. C., & Zmuda, J. M. (1997). A collection of physical activity questionnaires for health-related research. Medicine and Science in Sports and Exercise, 29, s1-s205.

Pichot, V., Roche, F., Gaspoz, J., Enjolras, F., Antoniadis, A., Minini, P., Costes, F., Busso, T., Lacour, J., & Barthelemy, J. C. (2000). Relation between heart rate variability and training load in middle-distance runners. Medicine and Science in Sports and Exercise, 32, 1729-1736.

Spinelli, L., Petretta, M., Marciano, F., Testa, G., Rao, M. A. E., Volpe, M., & Bonaduce, D. (1999). Cardiac autonomic responses to volume overload in normal subjects and in patients with dilated cardiomyopathy. American Journal of Physiology, 277, H1361-H1368.

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. (1996). Heart rate variability: standards of measurement, physiological interpretation, and clinical use. Circulation, 93, 1043-1065.

Tsuji, H., Larson, M. G., Venditti, F. J., Manders, E. S., Evans, J. C., Feldman, C. L., & Levy, D. (1994). Impact of reduced heart rate variability on risk for cardiac events: The Framingham Heart Study. Circulation, 94, 2850-2855.

Wilmore, J. H., Stanforth, P. R., Gagnon, J., Rice, T., Mandel, S., Leon, A. S., Rao, D. C., Skinner, J. S., & Bouchard, C. (2001). Heart rate and blood pressure changes with endurance training: The HERITAGE Family Study. Medicine and Science in Sports and Exercise, 33, 107-116.

Winder, W. W., Hagberg, J. M., Hickson, R. C., Ehsani, A. A., & McLane, J. A. (1978). Time course of sympathoadrenal adaptation to endurance exercise training in man. Journal of Applied Physiology, 45, 370-374.

Yamamoto, K., Miyachi, M., Saitoh, T., Yoshioka, A., & Onodera, S. (2001). Effects of endurance training on resting and post-exercise cardiac autonomic control. Medicine and Science in Sports and Exercise, 33, 1496-1502.

Yang, R. C., Mack, G. W., Wolfe, R. R., & Nadel, E. R. (1998). Albumin synthesis after intense intermittent exercise in human subjects. Journal of Applied Physiology, 84, 584-592.

Appendix A

Extended Review of Literature

Influence of Peak Aerobic Power and Exercise Endurance Training on Autonomic Regulation of the Cardiovascular System

Introduction

The heart and blood vessels are constantly challenged by a wide variety of stimuli (i.e. temperature, bodily movement, etc.). In order to respond to these challenges, the cardiovascular (CV) system is tightly regulated by the autonomic nervous system (ANS). The ANS helps regulate systemic arterial blood pressure (BP), cardiac function, body temperature, gastrointestinal motility, bladder emptying and other physiologic functions. It is an integral part of the properly functioning human body due to the rapidity and intensity with which it can alter physiologic processes. The ANS may be activated by control centers in the brain stem, spinal cord, hypothalamus, portions of the cerebral cortex, and by various reflex mechanisms that direct afferent signals to these control centers. Efferent signals are then transmitted throughout the body via either sympathetic or parasympathetic pathways.

Of primary importance to the human body is the proper functioning of the CV system. The CV system, consisting of the heart, blood, and vasculature, acts to provide the body with a continuous stream of nutrients and oxygen for energy and also allows for the removal of metabolic by-products. In 1870, Fick expressed CV function as an interplay between oxygen consumption (VO_2), cardiac output (CO), and arteriovenous oxygen difference (a-vO_2diff). The "Fick equation" that describes the relationship between these factors is still used to grossly describe CV functionality and is a useful index of work: $VO_2 = CO * a\text{-}vO_2diff$. CO is regulated by multiple mechanisms, including factors affecting both heart rate (HR) and stroke volume (SV) (i.e. preload, afterload, etc.). Lakatta and Maughan (1990) described multiple factors that help determine cardiovascular performance (Table 1.1) and provide a detailed review of CV function. Thus, the accurate quantitative description of CV function

would require a polynomial equation with at least as many terms as the number of factors listed in Table A.1. Each of these factors is subject to autonomic modulation, which forms the basis of many CV reflexes.

Table A.1

Some Determinants of Cardiovascular Performance.

Cardiovascular system properties	**Cardiac muscle properties**
Ventricular performance	Myocyte properties
Pericardial properties	Nonmyocyte properties
Arterial properties	Nutrient supply and waste removal
Venous properties	Cell-length
Blood properties (i.e. volume, viscosity)	Collagen strain
Body properties	
Intrathoracic pressure	**Cardiac myocyte properties**
Heart rate	
	Myofilament properties
Cardiac ventricular properties	Excitation properties
	Myofilament activation
Myocardial properties	Sarcomere length
Activation sequence	Cross-bridge number
Coronary vascular properties	Cross-bridge activation
Afterload system properties	Intracellular skeleton
Preload system properties	Organelle phosphorylation
Valves	Oxygen and substrate supply
Intrachamber communication	Adenosine triphosphate production

The cardiovascular control center (CVC) is found in the reticular formation of the brain stem, primarily located in the pons and medulla oblongata. The CVC receives afferent signals from various receptors throughout the body (feedback) or from higher nervous centers such as the motor cortex (feedforward) and respond by sending efferent impulses to various systems of the body. Within the CVC, there are both cardiac and vasomotor centers controlling cardiac and peripheral blood vessels, respectively. Within the cardiac center, a cardioinhibitory center is found in nucleus ambiguus and dorsal nulceus of the vagus nerve.

As its name implies, vagal efferents from these sites act to decrease both heart rate and contractility. Conversely, a cardiostimulatory center is believed to be located in the lateral medulla and function to increase heart rate and contractility via sympathetic activity. Within the vasomotor center, a vasoconstrictor area of the medulla is believed to be involved in sympathetic vasoconstriction of blood vessels. The presence of an opposing vasodilator area is questionable and vasodilation may be simply the result of inhibition of the vasoconstrictor area (Smith & Kampine, 1990).

Preganglionic nerves of the sympathetic nervous system (SNS) originate in the gray matter of spinal segments T-1 through L-2 and pass through the anterior root of the spinal cord into the corresponding spinal nerve. The preganglionic fibers then enter one of two paravertebral chains of ganglia. From there, fibers can synapse with postganglionic neurons in the paravertebral ganglia, follow ascending or descending pathways in the chain to synapse in other ganglia of the paravertebral chain, or pass out of the paravertebral chain and terminate in one of the prevertebral ganglia. The postganglionic nerves therefore originate in either the paravertebral or prevertebral ganglia and travel to destinations throughout the body. There are also preganglionic fibers that traverse, without synapsing, all the way to the adrenal medulla and cause the release of catecholamines (epinephrine and norepinephrine) into the blood.

Preganglionic nerves of the parasympathetic nervous system (PNS) leave the central nervous system via cranial nerves III, VII, IX, and X and sacral spinal nerves 1-4. Approximately 75% of PNS fibers are in the vagus nerves (cranial nerve X) supplying the heart, lungs, esophagus, stomach, small intestine, colon, liver, gall bladder, pancreas, and ureters. Most preganglionic nerves of the PNS pass uninterrupted to the target organ. In the

wall of the target organ, preganglionic fibers synapse with short postganglionic fibers that spread throughout the organ.

Preganglionic fibers of both the SNS and PNS stimulate postganglionic neurons by secreting the neurotransmitter acetylcholine (ACh) and therefore are classified as cholinergic. Furthermore, all postganglionic fibers of the PNS are cholinergic. In contrast, most postganglionic neurons of the SNS secrete the neurotransmitter norepinephrine (NE) and are classified as adrenergic. Exceptions include the sympathetic postganglionic fibers of the sweat glands, piloerector muscles, and some blood vessels that are cholinergic. As previously mentioned, the adrenal medulla acts as a postganglionic neuron in that some preganglionic neurons of the SNS innervate the adrenal medulla and cause the release of epinephrine (E) and NE into the circulation.

Autonomic neurotransmitters bind with specific receptors on the cell membrane of the effector organ. When the transmitter binds, the receptor changes its conformation and generally acts by either altering cell membrane permeability to ions, or by activating or inactivating intracellular enzymes. There are two types of cholinergic receptors found within the ANS. Nicotinic ACh receptors are located on the dendrites and cell bodies of all postganglionic neurons of both the SNS and PNS, while muscarinic ACh receptors are found on all effector organs of the PNS and those of the SNS that are stimulated by cholinergic neurons. There are also two major types of adrenergic receptors within the ANS, alpha and beta. Alpha and beta receptors are further subdivided into $alpha_1$, $alpha_2$, $beta_1$, $beta_2$, and $beta_3$ receptors. Catecholamines have somewhat different effects on alpha and beta receptors. E stimulates both alpha and beta equally, while NE excites predominantly alpha, and to a lesser extent beta receptors. Thus, the effect of catecholamines on various organs depends on

the receptor distribution. The location and responses to stimulation of the adrenergic receptors are described in Table A.2.

As described in Table A.2, complete understanding of SNS and PNS function on effector organs requires one to inspect the effect of each branch of the ANS on each organ individually. With regard to the CV system, SNS stimulation generally increases the activity of the heart by increasing both HR and contractility, while the PNS acts oppositely. Therefore, the SNS acts to increase the efficiency of the heart during periods of stress, whereas the PNS is more predominant during resting conditions. Sympathetic stimulation results in the constriction of most blood vessels via alpha receptors while PNS activation has little or no effect, although in some instances SNS activation results in a beta receptor-mediated vasodilation. Since BP is a product of CO and total peripheral resistance (TPR), SNS stimulation elevates BP by increasing both CO and TPR. Activation of the PNS usually results in a slight decrease in BP as a result of diminished cardiac performance, and extreme levels of parasympathetic activity may result in the cessation of cardiac activity causing a drastic loss of BP.

The design of the ANS provides the human body with the means to maintain a state of homeostasis in the face of various physiological challenges. Modulation of the ANS is largely attributed to the presence of various autonomic reflexes. Receptors that respond to stretch, chemical stimuli, temperature, and pain are located throughout the body and activate these reflexes. However, due to limited influence on the CV system, pain-sensitive free-nerve endings will not be discussed further in this review. Arterial baroreceptors are located in the walls of the aortic arch and internal carotid arteries. These stretch-sensitive receptors are innervated by afferent fibers that connect with vagus and glossopharyngeal nerves and relay

Table A.2

Locations and Responses of Adrenergic Receptors.

Receptor	Locations	Effects of stimulation
$Alpha_1$	Smooth muscle fibers of blood vessels; radial muscle of iris; sphincter muscles of stomach and urinary bladder	Excitation → contraction, leading to vasoconstriction, dilation of pupil, and closing of sphincters
	Salivary gland cells	Secretion of potassium and water
	Sweat glands on palms and soles	Increased sweating
$Alpha_2$	Smooth muscle fibers in blood vessels	Inhibition → relaxation → vasodilation
	Beta cells of pancreatic islets	Decreased insulin secretion
	Blood platelets	Platelet aggregation
$Beta_1$	Cardiac muscle fibers	Excitation → increased force and rate of contraction
	Juxtaglomerular cells of kidney	Renin secretion
	Posterior pituitary gland	Secretion of antidiuretic hormone
	Adipose cells	Breakdown of triglycerides → release of fatty acids into the blood
$Beta_2$	Blood vessels supplying skeletal muscle, adipose tissue, liver, and heart; smooth muscle in walls of airways; walls of visceral organs	Inhibition → relaxation, leading to dilation of airways, vasodilation, relaxation of organ walls
	Liver hepatocytes	Glycogenolysis
$Beta_3$	Brown adipose tissue	Thermogenesis

impulses to the CVC. In response to stretch (due to changes in arterial pressure), these receptors initiate action potentials of a frequency proportional to the magnitude of the stretch. Upon reaching the CVC, the action potential elicits an appropriate response. For example, a decrease in BP detected by the baroreceptors results in an activation of the cardiostimulatory and vasoconstrictor areas, along with an inactivation of the cardioinhibitory areas of the CVC. This in turn increases heart rate, contractility, and vasoconstriction, which result in increased BP. Conversely, this negative feedback mechanism acts oppositely for an increase in blood pressure.

In general, the aortic and carotid baroreceptors function synergistically. However, the aortic baroreceptors operate over a higher range of arterial pressures than the carotid baroreceptors and account for the majority (approxiamtely two-thirds) of the arterial baroreflex response. Interestingly, Donald and Edis (1971) demonstrated that both carotid and aortic baroreceptors are more sensitive to changes in blood pressure at physiological ranges (80-150 mmHg). In addition, baroreceptors respond more readily to decreases than to increases in blood pressure. In cases of chronic or acute alterations in baseline blood pressure, baroreceptors have the capability to "reset", or alter their own baseline to higher levels.

Other low-pressure baroreceptors are located in the walls of the heart and pulmonary vessels and are collectively referred to as cardiopulmonary baroreceptors. Cardiopulmonary baroreceptors are located within the venoatrial junctions, atria, ventricles, and pulmonary vessels (Edis, Donald, & Shepher, 1970; Paintal, 1973). These baroreceptors are primarily subserved by the afferent vagus limb (Oberg & White, 1970; Paintal, 1973) that constantly exerts a tonic restraint on the CVC. Stimulation of the cardiopulmonary baroreceptors by

hypervolemia or increased central venous pressure results in an enhancement of this tonic restraint and a subsequent peripheral vasodilation (Echt, Duweling, Gauer, & Lange, 1974). This vasodilation appears to be mediated via an inhibition of sympathetic efferent nerve activity and helps maintain arterial pressure and prevent the disturbance of the arterial baroreceptors. Under conditions in which the cardiopulmonary baroreceptor-mediated vasodilation is unable to accommodate increases in central volume and cannot maintain arterial pressure, the arterial baroreflex will take over and allow for the vasodilatory effect. Additionally, cardiopulmonary baroreceptors have the capability to elicit a peripheral vasoconstriction, via elevated sympathetic outflow, in response to periods of central hypovolemia.

Other receptors in the body regulating CV activities are sensitive to chemical stimuli. Central chemoreceptors located just beneath the ventral surface of the medulla are sensitive to changes in cerbrospinal fluid composition and blood chemistry. These receptors respond primarily to the partial pressure of carbon dioxide (PCO_2) and hydrogen ion (H^+) concentration. Stimulation of central chemoreceptors results in increased strength of both the inspiratory and expiratory signals to respiratory muscles and does not have a pronounced effect on the cardiovascular system. Peripheral chemoreceptors located in the carotid and aortic bodies respond not only to changes in PCO_2 and H^+, but are also sensitive to decreases in the partial pressure of oxygen (PO_2) and increases in arterial potassium (K^+) concentration. In humans, greater emphasis is placed on the chemoreceptors of the carotid bodies, as the aortic bodies are believed to be inactive (Nye, 1994). Carotid body chemoreceptors are located at the bifurcation of the carotid artery where they can sample blood composition prior to the perfusion of the brain. These chemoreceptors are composed of both type-I and type-II

cells. Type-I cells appear to be the sensors of arterial blood and make synaptic contact with sensory nerves leading to the carotid sinus nerve. The neurotransmitter activating the sensory nerves is not known, but is thought to be either a catecholamine (Fidone & Gonzales, 1986) or substance P (Prabhakar et al. 1989). The type-II cells envelope the type-I cells and sensory nerve endings and are believed to control the ionic environment of the synapse between the type-I cells and the sensory nerves. Sympathetic nerves innervate blood vessels of the carotid body and are thought to decrease blood flow and therefore excite the chemoreceptors by increasing the concentration of metabolic byproducts. Sympathetic nerves also appear to innervate the type-I cells, leading researchers to believe that the chemoreceptors can be activated independent of changes in blood flow or composition.

Carotid chemoreceptor stimulation, via experimentally-induced hypoxia or hypercapnia, has been shown to evoke bradycardia in several species, including humans (Jain, Subramanian, Julka, & Guz, 1972; Marshall, 1994). Furthermore, removal of the carotid bodies in humans has been shown to elicit a tachycardic effect (Gross, Whipp, Davidson, Koyal, & Wasserman, 1976; Honda, Hashizume, Kimura, & Severinghaus, 1988). The chemoreceptor-induced bradycardia is most probably mediated via the vagus nerve (Daly & Kirkman, 1989; Daly & Scott, 1958; Daly & Scott, 1962;), while a decreased sympathetic component may also play a minor role (Schmidt, Ledderhas, & Honig, 1985). Chemoreceptor stimulation has also been reported to have a negative inotropic effect on the heart mediated by either a sympathetic withdrawal (Hainsworth, Karim, & Sofola, 1979) or vagal activation (De Geest, Levy, & Zieske, 1965). Cardiac output also is reduced by chemoreceptor activation, most probably a result of the bradycardic effect (Daly & Scott, 1963). Carotid chemoreceptor stimulation also results in a vasoconstriction in the coronary arteries (Vatner & McRitchie,

1975), skeletal muscle arterioles (Oberg, 1964), and the small vessels of the cutaneous circulation (Calvelo, Abboud, Ballard, & Abdel-Sayed, 1970), likely via increases in sympathetic noradrenergic activity.

Mechanical and chemical receptors are also located in skeletal muscle tissue. Four groups of sensory afferent neurons arise from skeletal muscle. Groups I, II, and III are ensheathed within myelin, while group IV afferents are unmyelinated. Groups I and II are relatively large in diameter (6-20 um) and have conduction velocities $\geq$30 meters$\bullet$second^{-1}. Group I and II afferents do not play a role in chemoreception or CV control and so will not be dealt with in this review (Waldrop, Rybicki, & Kaufman, 1984). Conversely, group III and IV are smaller in diameter (1-6um) and have slower conduction velocities (<15 meters$\bullet$second^{-1}). Group III nerve endings seem to be associated with collagen structures within the skeletal muscle, while group IV endings are associated with blood and lymphatic vessels (von During, Andres, & Schmidt, 1984). The types of stimuli to which these muscle afferents primarily respond are reflected in the terminology by which they are described. Group III nerve endings are primarily activated by deformation changes and are termed mechanoreceptors, whereas group IV afferents primarily respond to changes in metabolic by-products (i.e. lactic acid, arachidonic acid, potassium, bradykinin) and are termed metabo- or chemoreceptors (Mitchell & Schmidt, 1983). However, the separation between the two is not perfect as a portion of mechanoreceptors respond to metabolites and a portion of metaboreceptors respond to mechanical stimuli. Group III and IV afferents synapse in the dorsal horn of the spinal cord, ultimately activating the cells of ascending tracts that project to the medulla. These receptors play a major role in the exercise pressor reflex, a feedback mechanism to the CVC originating in skeletal muscle that results in a reduced

parasympathetic and increased sympathetic outflow to the cardiovascular system during exercise.

There are also temperature-sensitive receptors located either peripherally in the skin or deep in the abdominal viscera and spinal cord. Interestingly, there are far more cold-sensitive than heat-sensitive receptors, likely reflecting an effort to prevent hypothermic conditions in the body. In response a hot environment, the body exhibits a vasodilation of cutaneous blood vessels mediated by a sympathetic inhibition in an attempt to transfer heat to the skin. On the other hand, a cold stimulus results in a sympathetic-mediated cutaneous vasoconstrition in an attempt to reduce heat loss through the skin (Guyton & Hall, 1994).

As previously stated, the CVC is also under the influence of higher nervous centers. Central command consists of centrally generated nerve activity that activates, either in parallel or separate neural pathways, the CV and skeletal muscle motor systems (Rowell, 1986). Signals may originate in the motor cortex, basal ganglia, cerebellum, or spinal cord. The traditional view of central command as proposed by Krogh and Lindhard (1913) consists of motor signals arising from the cerebral cortex acting directly on the CVC and autonomic preganglionic cells controlling the heart and vasculature. More recent researchers have provided evidence that the subthalamic area and cerebellum may also play a role in generating CV and respiratory responses (Eldridge, Millhorn, Kiley, & Waldrop, 1985; Rowell, 1993; Smith, Rushmer, & Lasher, 1960).

The hypothalamus also plays a role in the regulation of body activities. As a key regulator of homeostasis, sensory impulses arrive at the hypothalamus via afferent pathways along with impulses from hearing, taste, and olfactory receptors. Other receptors within the hypothalamus monitor osmotic pressure, hormone concentration, and temperature.

Specifically regarding CV regulation, neuronal axons extend from the hypothalamus to sympathetic and parasympathetic nuclei in the brain stem and spinal cord and can exert influence on CV activity. The hypothalamus also influences the release of several hormones from the pituitary gland that may influence the CV system.

There exists evidence, both for and against, an influence of CV fitness, as defined by VO_{2peak}, and exercise endurance training on the ANS. When investigating these issues, however, it is imperative to control for possible mitigating factors such as age, gender, race, environmental conditions, that may also impact autonomic regulation of the CV system. Therefore, the objectives of this review are as follows: 1) to briefly describe some of the current techniques of quantifying autonomic activity, 2) to review evidence for autonomic control of the CV system during an acute bout of rhythmic exercise involving large muscle groups, 3) to discuss several mitigating factors that may influence autonomic regulation of the CV system, 4) to review literature that has examined the influence of aerobic fitness, as estimated by peak oxygen consumption, on autonomic regulation of the CV system estimated by the previously mentioned techniques, and 5) review literature that has examined the influence of exercise endurance training on autonomic regulation of the CV system estimated by these techniques.

Evaluating Autonomic Control

Cardiovascular responses to laboratory stressors. The assessment of HR and BP reactivity to stressful stimuli in a controlled environment are commonly used to investigate autonomic control of the circulation (Grassi et al.1996). Stressful stimuli can be physical, as in the cold-pressor test or isometric exercise, or psychological, as in the Stroop color-word conflict task (CWCT) or other mental tasks. Methods using hemodynamic reactivity to assess autonomic

control are based on the assumption that whenever the HR or BP effects are greater than normal, the SNS is hyperactive and/or there is some degree of vagal withdrawal (Mancia, & Grassi, 1991). However, these techniques are not without their limitations. For example, there is evidence that vascular hypertrophy amplifies the effects of smooth muscle constriction. Therefore, an elevated pressor response may be secondary to structural factors rather than autonomic abnormalities (Folkow, 1982). Other limitations relate to the generalizability and reliability of these responses. For example, it has been demonstrated that CV hyperresponsiveness to laboratory stress may not reflect a hyperreactivity to normal "real-life" stressors (Parati et al. 1988). Moreover, CV responsiveness is not always consistent across various laboratory stressors (Parati, Pomidossi, Ramirez, Cesana, & Mancia, 1985). Lastly, HR and BP reactivity to laboratory stimuli exhibit considerable within-subject variability (Mancia & Grassi, 1991; Parati et al. 1985; Swain & Suls, 1996). Swain and Suls published an excellent meta-analytic review regarding the reproducibility of HR and BP reactivity to laboratory stressors. By reviewing 24 studies, they report overall correlation coefficients of 0.555 for HR, 0.407 for systolic BP (SBP), and 0.348 for diastolic BP (DBP). Furthermore, the reproducibility of HR and SBP were much better for studies with shorter test-retest periods (<1 week) than for those with longer periods (>1 month), whereas DBP varied in a non-uniform manner. Other findings of this review are that older subjects exhibit better BP reproducibility than younger subjects and that BP reproducibility is greater in those tasks that do not involve vocal effort. In general, these findings suggests that results obtained from hemodynamic reactivity to laboratory stressors need to be interpreted cautiously, with regards to test-retest length, subject age, and stressor type.

Assessment of catecholamine concentration. Plasma NE is frequently used as an indicator of SNS activity under various conditions, as it is the major neurotransmitter of the SNS. A percentage of NE spills over from terminal nerve endings into the circulation, making its concentration 3-4 times higher than that of E at rest (Esler et al. 1990). The chromaffin cells of the adrenal medullas are the primary source of plasma E and are under direct sympathetic control, although they may be activated by acute conditions such as hypoglycemia (Esler et al. 1990). Therefore, the assessment of catecholamines has been an important tool in investigating the sympathetic branch of the autonomic nervous system.

Several different techniques have been developed to assess plasma catecholamines. These include plasma and tissue concentrations of catecholamines, release, clearance, spillover into plasma, intrasynaptic NE concentration, neuronal NE uptake, and urinary excretion. See Esler et al. (1988) for a review. However, some of the more commonly used methods, (plasma NE concentration, NE clearance, and NE spillover), deserve a brief review here.

Plasma NE is the most commonly used index of sympathetic tone in man (Mancia & Grassi, 1991). Physiological conditions or perturbations that alter sympathetic drive are reflected by changes in NE concentration. However, plasma NE concentration reflects two concurrent processes, its appearance (or spillover) into the plasma after release from sympathetic nerve endings, and its clearance from the circulation. Therefore, examination of plasma NE kinetics provides a more sensitive index of SNS activity than measuring plasma concentrations alone. This has led to the development of techniques using radiolabelled NE to assess NE clearance and the "spillover rate" of NE into the plasma, assuming steady-state conditions hold. (Esler, 1982; Poehlman, McAuliffe, & Danforth, 1990). The same

techniques can also be used for examination of the kinetics of E released from the adrenal medulla (Kjaer, Christensen, Sonne, Richter, & Galbo, 1985).

NE plasma clearance rate ($l \bullet min^{-1}$) =

[^{3}H] NE infusion rate / plasma [^{3}H] NE concentration

NE spillover rate ($ug \bullet min^{-1}$) =

[^{3}H] NE infusion rate / specific radioactivity of plasma NE

or *NE clearance rate * plasma NE concentration*

Although the measurement of the NE spillover rate is a valid method to assess the activity of sympathetic effector-junctions, it is not without its limitations. For example, the exact source of the NE release is not identified, although in humans there is good agreement that the sympathetic nerves of the kidneys, skeletal muscles, and lungs all contribute substantially (Esler et al. 1988). Moreover, some vascular beds may contribute significantly more NE than others and may exhibit differential adrenergic receptor densities making it an unbalanced and/or insensitive index (Mancia & Grassi, 1991). Lastly, Hjemdahl (1984) reported that plasma NE measurements suffer from poor inter- and intralaboratory reproducibility, possibly a result of the wide variety of assay techniques available, and would benefit from better standardization and continuous quality control.

Muscle sympathetic nerve activity. The use of microneurography to directly measure sympathetic nerve activity to muscle (MSNA) in humans was first developed by Hagbarth and Valbo (1968). This method detects raw action potentials via tungsten microelectrodes inserted under the skin at one of several possible sites. The action potentials are then amplified, filtered, and integrated, yielding a mean voltage neurogram (Rothman, Easty, Frecker, & Floras, 1991). Sympathetic bursts on the neurogram are abolished by

pharmacologic blockade of sympathetic ganglia and local anesthesia applied to the nerve proximal, but not distal to the recording site. Furthermore, the conduction velocity of the bursts are ~ 1 meter • second^{-1}, the same velocity of unmyelinated nerve fibers in animals (Mitchell & Schmidt, 1983). Finally, studies have demonstrated a close positive relationship between MSNA (expressed as burst • min^{-1}) and plasma NE levels (Leimbach et al. 1986; Wallin et al. 1981; Yamada, Miyajima, Tochikubo, Hatsukawa, & Ishii, 1989). Therefore, the neurogram is believed to reflect sympathetic nerve activity to the skeletal muscle bed. The use of microneurography to detect MSNA has been useful to many researchers by providing insight into the neural regulation of the circulation at rest and during perturbations that alter sympathetic outflow (Ray & Hume, 1998).

MSNA has traditionally been quantified by visual inspection of the mean voltage neurogram. Using visual inspection, the observer spots the bursts of activity by searching for triangular peaks with a "smooth envelope" rising from a noisy baseline. Average inter- and intra-observer variabilities of 4% and 9%, respectively, have been reported by Mark and Victor (1985) for this technique. However, the subjective and labor-intensive process of visually inspecting peaks may be inferior to more recently developed automated techniques that are faster and objective.

Several automated techniques have been used to evaluate MSNA in humans. Rea, Birckett, Hamdam, and Mark (1989) developed a burst averaging technique to quantify MSNA. Several researchers have also developed peak detection algorithms to quantify sympathetic bursts (Ebert, 1988; Rothman, Easty, Frecker, & Floras, 1991; Wallin & Eckberg, 1982). By comparing burst averaging to visual inspection, Rothman et al. (1991) reported that manual interpretation of MSNA overestimated sympathetic activity by an

average of 112 units/min, or 19%. This group further reported that visual inspection overestimated MSNA by 183 units/min, or 31% compared to the use of a peak detection algorithm. However, there was only a 70.6 unit/min difference between burst averaging and the peak detection technique.

The use of MSNA to quantify sympathetic outflow to the muscle has shown high intra-individual reproducibility (Fagius & Wallin, 1993; Fagius & Wallin, 1983; Sundlof & Wallin, 1977; Yamada, Miyajima, Tochikubo, Matsukawa, & Ishii, 1989). For example, Fagius and Wallin (1993) reported high long-term reproducibility (10-14 yr) of MSNA in adults. This group reported correlation coefficients of 0.81 and 0.90 for MSNA expressed as bursts•min^{-1} and bursts•100 heart beats^{-1}, respectively, between recordings. Yamada et al. (1989) demonstrated good short-term (3-20 days) reproducibility of MSNA expressed as bursts•min^{-1} (r=0.88), bursts•100 heart beats^{-1} (r=0.84), and spike frequency (r=0.84). Fagius and Wallin (1983) also demonstrated exceptional reproducibility over a test-retest period of 2 days to 4 years (r=0.94), while Sundlof and Wallin (1977) reported little differences in MSNA measures repeated over 3 weeks to 21 months (range of differences = 0.5-11.2 bursts•100 heart beats^{-1}).

However, MSNA measures have been reported to vary considerably between healthy individuals making it difficult to establish normality criteria at rest (Fagius & Wallin, 1993; Sundlof & Wallin, 1978; Sundlof & Wallin, 1977). For example, resting MSNA in healthy individuals is commonly found within the range of 1-60 bursts•min^{-1} (Fagius & Wallin, 1993). This wide range makes it difficult to determine differences among groups and could possibly give rise to false observations. Therefore, data obtained from MSNA may be most appropriate for repeated measures designs.

Heart rate variability. Homeostasis does not imply rigidity, but rather that physiologic systems operate within specific limits that allow oscillations around mean optimal values. Such behavior is observed even under steady state conditions, as exemplified by beat-to-beat fluctuations in heart period. Heart rate variability (HRV) has recently become a popular noninvasive tool to estimate cardiac autonomic modulation (Malik, 1998), because it is easily measured and is a fairly straightforward index of autonomic control. Analysis of these fluctuations has been useful in providing information regarding the physiology of the active autonomic control branches (Akselrod et al. 1981; Pomeranz et al. 1985). Advantages to analyzing these fluctuations include obtaining physiologic information noninvasively and without interfering with neural functions of the control mechanisms.

In the most basic form, HRV may be expressed as a time domain measure. This often includes the computation of the variance of a series of RR intervals around the mean heart period. The most commonly used time domain measure is the standard deviation of normal-to-normal RR intervals (SDNN), which reflects all of the cyclic components accountable for the variability of the HR during the recording period. Other common time domain variables include the following: the standard deviation of the average RR intervals calculated over 5-minute segments (SDANN), the mean of the 5-minute standard deviations of normal RR intervals calculated over 24-hours (SDNN index), the square root of the mean squared differences of successive RR intervals (rMSSD), the number of pairs of adjacent RR intervals differing by more than 50 ms (NN50), and the percentage of NN50 relative to all RR intervals (pNN50). Although these measures are able to provide an estimate of the overall variability in the HR, such measures neglect important information, namely the frequency content of the

variations (Task Force of the European Society of Cardiology and the North American Society for Pacing and Electrophysiology, 1996).

As a result, frequency domain methods (spectral analysis) have been adopted, usually consisting of algorithms for the computations of power spectra of heart rate. This method has yielded he most promise regarding the amount and specificity of the information obtained from HRV. Spectral analysis of HRV may be performed by two different methods: a technique focusing on "fast" HR oscillations (<30 seconds), and a "broad band" technique which considers all components of variability within a given recording time (minutes to hours). Since most research has centered on the fast fluctuations of HR, broad band spectral analysis will not be further dealt with in this review. The two most commonly used algorithms used for spectral analysis of fast HR fluctuations are the fast Fourier transformation (FFT) and autoregressive (AR) modeling. The spectrum derived from the FFT includes the entire signal variance, regardless of whether the power appears as peaks or as broadband (non-peaked) powers. Conversely, the AR algorithm identifies a best-fitting model for the raw data from which the final spectrum, consisting of a variable number of peaks, is derived (Parati, Saul, Di Rienzo, & Mancia, 1995).

Spectral analysis techniques used to quantify HRV focus on the frequency components between 0.025 and 0.5 Hz, as this range of power has been reported to reflect neural autonomic influences (Akselrod et al. 1981; Malliani, Pagani, Lombardi, & Ceruti, 1991). Rosenblueth and Simeone (1936) demonstrated long ago that whereas slow heart rate fluctuations are mediated by both sympathetic and parasympathetic control, sympathetic activity is unable to mediate faster heart rate changes. Therefore spectral analysis, by separating components by their frequency, should be able to discriminate between frequency

ranges to which slow and faster mechanisms contribute (vagal activity should be expressed at a higher frequency). It was in fact later determined that vagal cardiac control can modulate the HR up to 1.0 Hz, while sympathetic outflows to the heart can only modulate the HR at frequencies below 0.15 Hz. The power spectra bands have been further divided into the following ranges: high-frequency (HF) (0.15 – 0.4 Hz), low-frequency (LF) (0.04 – 0.15 Hz), very low-frequency (VLF) (0.003 – 0.04 Hz), and ultra low-frequency (ULF) (0.0 – 0.003 Hz) (Task Force of the European Society of Cardiology and the North American Society for Pacing and Electrophysiology, 1996).

The HF peak is thought to be an indicator of vagal modulation and is commonly referred to as the respiratory peak as it corresponds to the heart rate variations related to the respiratory cycle (Parati et al. 1995). Studies using the vagal blocker atropine have demonstrated a dose-dependent reduction in the HF peak, leaving power below 0.15 Hz partly unaffected (Eckberg, 1983; Katona & Jih, 1975; Saul et al. 1991). Therefore, the HF component of the power spectrum is often used as a measure of the integrity of vagal control. Conversely, the control mechanisms reflected by power in the LF range are not as well understood. Studies have shown that power between 0.04 and 0.15 Hz are reduced by both parasympathetic and sympathetic blockade. Furthermore, power of these lower frequencies has been associated with a wide variety of stimuli including thermoregulation, periodic breathing, and hemodynamic instability. Therefore, it appears that power in the LF range reflects sympathetic and parasympathetic control of the heart along with other mechanisms. Although there is usually a large amount of power in the VLF and ULF ranges, their physiological correlates still remain unknown.

HRV during resting conditions has generally been reproducible (Table 2.1). For example, Huikuri et al. (1990) analyzed the SDNN index over 2 consecutive 24-hour periods and 1 week apart in healthy adults. The authors grouped all data together and reported an interindividual coefficient of variation (COV) of 24% and an intraindividual COV of 7±6%. However, recalculation of the intraindividual COV for separate time periods results in the day-to-day variation being lower (COV: 4.2±3%) than that of the 1-week period (COV: 7.3±7%). Hohnloser, Klingenheben, Zabel, Schroder, and Just (1992) showed good reproducibility of time and frequency domain parameters on days 7 and 28 in healthy subjects with intraclass correlation coefficients (ICC) between 0.63 and 0.93. Kleiger et al. (1991) also reported good reproducibility of time and frequency measures of HRV between 3 and 60 days apart, with all of the ICC's above 0.84 with the exception of SDNN (ICC=0.7). Regarding clinical populations, Van Hoogenhuyze et al. (1991) and Piepoli et al. (1996) both demonstrated good reproducibility in patients with heart failure. Bigger, Fleiss, Rolnitzky, and Steinman (1992) found remarkable stability of HRV measures in post-myocardial infarction patients on day 7 with ICCs >0.79. In diabetic populations, Nolan et al. (1996) reported an ICC of 0.91 for pNN50, while Burger, Charlamb, Weinrauch, and D'Elia (1997) showed good short and long-term reproducibility of HRV measures.

Blood pressure variability. Similar to heart rate, blood pressure exhibits beat-to-beat fluctuations. Blood pressure variability (BPV) has been widely assessed by calculating the standard deviation of the mean of SBP, DBP, and mean arterial pressure (MAP) from a 24-hour tracing. However, this technique is associated with several limitations. For example, the 24-hour signal has non-stationary components more suitable to nonparametric than to parametric methods of signal analysis such as the standard deviation (SD). Also, 24-hour

Table A.3

Test-Retest Reliabilities of Commonly Measured Indices of Heart Rate Variability

Author/Date	Population (age)	Acquisition length	Test-retest period	Variable	CV	r
Bigger et al. (1992)	Post-MI (59±11 yr)	24-hr	7-days	TP	---	0.90
				HF	---	0.92
				LF	---	0.96
Burger et al. (1997)	IDDM (37±10 yr)	24-hr	3, 6, 9, & 12-months	SDNN	---	0.81 (3-mo), 0.84 (6-mo),
					---	0.47 (9-mo), 0.85 (12-mo)
				SDANN	---	0.74 (3-mo), 0.78 (6-mo),
					---	0.35 (9-mo), 0.83 (12-mo)
				pNN50	---	0.98 (3-mo), 0.99 (6-mo),
					---	0.81 (9-mo), 0.81 (12-mo)
				rMSSD	---	0.94 (3-mo), 0.92 (6-mo),
					---	0.72 (9-mo), 0.82 (12-mo)
				TP	---	0.78 (3-mo), 0.77 (6-mo),
					---	0.63 (9-mo), 0.47 (12-mo)
				HF	---	0.84 (3-mo), 0.79 (6-mo),
					---	0.65 (9-mo), 0.78 (12-mo)
				LF	---	0.93 (3-mo), 0.79 (6-mo),
					---	0.71 (9-mo), 0.82 (12-mo)

SDNN, SDANN, pNN50, rMSSD, SDNN index = see text
r=intraclass correlation coefficient
CV=coefficient of variation
nu=normalized units
HF=high-frequency power
LF=low-frequency power
TP=total power
IDDM=insulin-dependent diabetes mellitus
MI=myocardial infarction

Table Con'd.

Table A.3

Author/Date	Population (age)	Acquisition length	Test-retest period	Variable	CV	r
Freed et al. (1994)	Healthy (44-83 yr)	10-min	10-hr	TP	9%	0.75
				HF	11%	0.92
				LF	15%	0.74
Hohnloser et al. (1992)	Healthy (24±2.5 yr)	24-hr	1-week & 1-month	SDNN	---	0.78 (1-wk), 0.63 (1-mo)
				rMSSD	---	0.89 (1-wk), 0.83 (1-mo)
				pNN50	---	0.93 (1-wk), 0.78 (1-mo)
				TP	---	0.87 (1-wk), 0.83 (1-mo)
				HF	---	0.85 (1-wk), 0.80 (1-mo)
				LF	---	0.86 (1-wk), 0.81 (1-mo)
Huikuri et al. (1990)	Healthy (20-40 yr)	24-hr	1 & 7 days	SDNN	7±6%	---
Kleiger et al. (1991)	Healthy (20-55 yr)	24-hr	3-65 days	SDNN	---	0.70
				pNN50	---	0.90
				rMSSD	---	0.90
				SDNN index	---	0.90
				TP	---	0.89
				HF	---	0.84
				LF	---	0.91

Table Con'd.

Table A.3

Author/Date	Population (age)	Acquisition length	Test-retest period	Variable	CV	r
Marks et al. (1999)	Healthy (27.5±6.3 yr)	5-min	1-week	SDNN	---	0.90
				HF	---	0.67
				LF	---	0.82
				LF:HF	---	0.86
Nolan et al. (1993)	Healthy (44±13 yr)	24-hr	2-weeks	pNN50	---	0.97
	Heart disease (58±7 yr)	24-hr	2-weeks	pNN50	---	0.94
	IDDM (52±12 yr)	24-hr	29, 63, 92, &115 days	pNN50	---	0.91 (29-d), 0.93 (63-d) 0.80 (92-d), 0.86 (115-d)
Piepoli et al. (1996)	Heart failure (64.3±5.4 yr)	5-min	3-weeks	SDNN	16%	0.78
				HF	14.5%	0.75
				HFnu	---	0.83
				LF	10%	0.79
				LFnu	---	0.83
				LF:HF	---	0.74

Table Con’d.

Table A.3

Author/Date	Population (age)	Acquisition length	Test-retest period	Variable	CV	r
Pitzalis et al. (1996)	Healthy (28±2 yr)	24-hr	2-weeks & 30-weeks	SDNN	---	0.57
				pNN50	---	0.78
				rMSSD	---	0.79
		10-min	2-weeks & 30-weeks	SDNN	---	0.56
				pNN50	---	0.40
				rMSSD	---	0.23
				TP	---	0.75
				HF	---	0.48
				LF	---	0.77
Sinnreich et al. (1998)	Healthy (31-67 yr)	6-min	2-months	SDNN	6.0%	0.77
				rMSSD	8.0%	0.75
				TP	7.0%	0.77
				HF	12.1%	0.76
				LF	11.5%	0.68
VanHoogenhuyze et al. (1991)	Heart failure (59±7 yr)	24-hr	1-day	SDNN	8.5%	0.97
				SDANN	13.8%	0.87

blood pressure values commonly are characterized by a non-normal distribution limiting the standard deviation to correctly reflect the shape of dispersion around the mean. Furthermore, the standard deviation lumps together different variability phenomenon, making it more difficult to single out different mechanisms of origination. Therefore, other techniques of assessing BPV have become popular.

Other techniques include the range of BP values measured over 24-hours, the difference between average day and night pressures, the difference between hourly BP means averaged for 24-hours, and power spectral analysis of BPV. Of these, power spectral analysis of BPV has shown the most promise. Similar to HRV, spectral analysis of BPV allows the splitting of variability phenomenon into various components of different frequencies of BP oscillations. Techniques that focus on fast oscillations in BP generally focus on frequencies between 0.025 and 0.5 Hz. Fluctuations in this range are thought to reflect the features of some cardiovascular control mechanisms. A clear peak is usually located at the respiratory frequency (~0.25-0.3 Hz), while other peaks are commonly found at ~0.1 and ~0.04 Hz. As with HRV, these peaks may be analyzed via a FFT or through AR techniques.

The HF (0.15-0.4 Hz) blood pressure component has been reported to reflect the mechanical effects of respiration on the pressure gradients, size, and functions of the heart and large thoracic vessels (Parati et al. 1995). It has also been reported that the vagally mediated changes in HR and CO contribute to the HF component of BPV (Parati et al.). Although the LF component (0.07-0.15 Hz) of BPV is not greatly affected by dual autonomic blockade with atropine and propranolol, it has been reported to increase with laboratory stimuli that increase sympathetic CV influences and decrease with those that decrease sympathetic influences. Therefore, it is believed that LF power represents a marker of sympathetic

vasomotor tone and systemic vascular resistance (Parati et al.). Frequencies between 0.025 and 0.07 Hz have been reported to reflect the renin-angiotensin system, endothelial factors, and local influences related to thermoregulation (Parati et al.).

There exist few studies that have specifically addressed the reproducibility of BPV measures. In general, studies that have assessed BPV by the SD have not been reliable. For example, Van Egeren and Sparrow (1989) reported ICCs of 0.11/0.00 (SBP/DBP) measured 1 month apart, while James et al. (1988) found ICCs of 0.18/0.22 measured 2 weeks apart. Furthermore, Gerin, Rosofsky, Pieper, and Pickering (1993) reported ICCs of 0.52/0.63 and 0.60/0.49 for SD and rMSSD, respectively, measured on 2 consecutive days. With regards to spectral indices of systolic BP, Taverner, Nunan, and Tonkin (1996) found poor reproducibility over days 1, 2, 3, 4, and 5 with CV's of 41 and 25% for LF/HF and LF power, respectively. Additionally, Dimier-David, Billon, Costagliola, Jaillon, and Funck-Brentano (1994) used Bland-Altman plots (Bland, & Altman, 1986) to assess the reproducibility of the HF and LF spectral components of systolic BP and reported good reproducibility between days 1 and 2 and between days 2 and 30.

Baroreflex sensitivity. Investigation of the cardiac baroreflex, which is concerned with the short-term regulation of arterial BP, has been used to gain insight into vagal and sympathetic control of the heart (Dawson et al. 1997). Baroreceptor sensitivity (BRS) was originally estimated in humans by assessing alterations in the pulse interval to pharmacologically-induced BP changes (Smyth, Sleight, & Pickering, 1969). Other methods of inducing cardiac baroreceptor activation that have been used include neck suction/pressure (Eckberg, Convertino, Fritsch, & Doerr, 1992), lower body negative pressure (LBNP) (Raven, Potts, & Shi, 1997), the Valsalva maneuver (Smith, Stallard, Salih, & Littler, 1987), and/or various

combinations of these. In all of these methods, the successive SBP values (measured intra-arterially) are correlated with the length of the next RR interval and the regression coefficient of the correlation gives the BRS in ms of RR interval per mmHg (Dawson et al., 1997; Robbe et al. 1987).

With the recent technology of beat-to-beat BP monitors and high-powered computers, BRS may now be assessed noninvasely. In sequence analysis, BP and RR intervals are measured over time and are evaluated for a sequence of ≥ 3 beats in which SBP and RR interval increase or decrease simultaneously. The threshold for a change in BP and RR interval is usually set at 1 mmHg and 4 ms, respectively. When there is a linear relationship between RR interval and SBP changes ($r \geq 0.85$), the slope of the regression line may be taken as an index of BRS (Dawson et al. 1997; Iida et al. 1999). Thus, the sequence method is analogous to invasive methods previously employed.

An even more recent method, the cross-spectral technique, uses power spectral analysis of HR and BP to quantify BRS (Iida et al., 1999; Pagani et al. 1988; Robbe et al., 1987). In this method, the square root of the ratio between the spectral powers of RR interval and SBP variabilities is termed the α-index and has been used as an index of BRS (Pagani et al.). The coherence function of the two spectra describes their linear dependence and only frequencies with a squared coherence greater than 0.5 are used to calculate the α-index (Pagani et al.). The α-indices may be computed for any frequency, but are usually computed for the LF and HF ranges as previously described (Dawson et al., 1997; Iida et al.).

Dawson et al. (1997) demonstrated good reproducibility of such noninvasive techniques to assess BRS. This group reported intra-individual CV's of 18.9% and 23.9% for BRS derived via α indices and the sequence technique, respectively, measured after 1 week

and 6 months. Furthermore, Iellamo et al. (1996) reported an intra-individual CV of 15% for the sequence technique assessed on two consecutive days.

Sympathetic skin response. It has been well documented that sympathetic skin activity stimulates the eccrine sweat glands of the body (Bini, Hagbarth, Hynninen, & Wallin, 1980; Hallin, & Torebjork, 1974; Torebjork, 1974). This physiological phenomenon has been used to quantify sympathetic nervous system activity to the skin. The sympathetic skin response (SSR), a change in voltage across the surface of the skin, and the classical Galvanic skin response, the change in skin resistance across the skin, have both been used as tools to investigate sympathetic skin activity (Shahani, Halperin, Boulu, & Cohen, 1984). These measures are usually assessed during electrical, physiological, or psychological stimuli. The nervous system pathway to the sweat glands is believed to begin in the posterior hypothalamus, traverse down the lateral columns of the spinal cord to preganglionic sudomotor neurons, and then to the postganglionic neurons that innervate the sweat glands (Gutrecht, 1994). Since most current research assessing electrodermal activity is performed by measuring SSR, the remainder of this section will focus on the techniques concerned with obtaining this measure.

Recordings of SSR are usually obtained from electrodes placed on the palm and dorsum of the hand and/or the sole and dorsum of the foot (Gutrecht, 1994). The type of stimulus used varies, although an electric shock (~10-30 mA) of approximately 0.1-0.2 ms duration is commonly used (Gutrecht). Skin temperature is also of concern as low temperatures may inhibit conduction of nervous impulses (Franz & Iggo, 1968). Thus, skin temperature is commonly maintained ≥ 32 degrees Celsius (Gutrecht).

The waveform obtained from the SSR may be biphasic or triphasic (Baba, Watahiki, Matsunaga, & Takebe, 1988) and is usually greater in the hand compared to the foot (Shahani et al. 1984). The magnitude of the waveform varies considerably between subjects and has been reported to habituate rapidly following repeated stimuli causing some researchers to use progressively increasing stimuli (Hoeldtke, Davis, Hshich, Gaspar, & Dworkin, 1992). However, the latency of the SSR (measured by stimulating the opposite side of the body) is not effected by repeated stimuli and is usually ~1.3-1.5 m/s at the hand and ~1.9-2.1 m/s at the foot (Shahani et al.).

Current data suggest that only an absent SSR should be considered abnormal due to the habituation and variability of responses (Hoeldtke et al. 1992). Additionally, caution must be used when attempting to use this methodology in the elderly as the SSR may not be elicitable in subjects > 60 years of age (Gutrecht, 1994). The clinical importance of SSR has been somewhat controversial. Although several studies have reported abnormal SSRs in various disease states including diabetic neuropathy (Soliven et al. 1987), familial amyloid polyneuropathy (Montagna, Salvi, & Liguori, 1988), chronic renal disease (D'Alpa, Scandurra, Lanaia, Scrofani, & Grasso, 1988), scleroderma (Raszewa, Hausmanowa-Petrusewicz, Blaszczyk, & Jablonska, 1991), Parkinson's disease (Johns, Gress, Shahani, & Young, 1986), and multiple sclerosis (Yokota, Matsunaga, Okiyama, et al., 1991), most of these findings are anecdotal and are not consistent. Therefore, more detailed studies comparing SSR to other clinical autonomic function tests are needed.

Autonomic Control During Rhythmic Exercise Involving Large Muscle Groups

At the onset of rhythmic exercise, several CV adjustments take place to meet the demands placed on the CV system. Heart rate and SV both increase resulting in an increased

CO and BP. Blood flow is directed towards active muscle and away from inactive tissues and the (a-v)O_2diff increases, reflecting an increase in oxygen transfer to the working muscles. In general, rhythmic exercise results in a parasympathetic withdrawal followed by a sympathetic activation. Many of these alterations are under the control of various autonomic regulatory mechanisms. Under the stress of rhythmic exercise, both central and peripheral autonomic reflex mechanisms initiate autonomic-mediated CV adjustments. This section will address autonomic behavior during acute submaximal rhythmic exercise involving large muscle groups.

Several studies have used HRV to examine the autonomic response to an acute bout of exercise (Table 3.1). Studies using spectral indices of HRV as an indicator of cardiac autonomic modulation have suggested a withdrawal of parasympathetic activity, as HF power is reduced with increasing exercise intensity (Arai et al. 1989; Brenner, Thomas, & Shepard, 1993; Casadei, Cochrane, Johnston, Conway, & Sleight, 1995; Kamath, Fallen, & McElvie, 1991; Perini, Milesi, Biancardi, Pendergast, & Veicsteinas, 1998; Perini, Orizio, Baselli, Cerutti, & Veicsteinas, 1990; Perini et al. 1993; Sekiguchi et al. 1979; Sun, Elken, & Mekjavic, 1993; Warren, Jaffe, Wraa, & Stebbins, 1997; Yamamoto, Hughson, & Peterson, 1991). It further appears that this decrease in HF power occurs at very light exercise intensities. For example, Yamamoto, Hughson, and Nakamura (1992) demonstrated a reduction in the HF component at <60% of the ventilatory threshold. Additionally, Perini et al. (1990) reported that HF power decreases during 5 minutes of upright cycling at 21% of aerobic power, while Perini et al. (1993) reported 6 minutes of supine cycling at 28% of maximal oxygen consumption was sufficient to significantly reduce HF power.

Table A.4

The Effects of Acute Dynamic Exercise on HRV Indices

Author/Date	Frequencies analyzed	Exercise (mode; duration; intensity)	Results
Casadei et al. (1995)	HF (0.14-0.60Hz) LF (0.04-0.14Hz)	cycle; 23 min; max incremental	HF ↓ (with ↑ int); HFnu ↓ (with ↑ int); LFnu ↓ (with ↑ int) until disappeared
Nakamura et al. (1993)	HF (0.15-0.80Hz) LF (0.00-0.15Hz) TP (0.00-0.80Hz)	cycle; NA; max incremental	HF:TP ↓ at >50%VO_{2max}; LF:HF ↑ up to 80% VO_{2max}
Arai et al. (1989)	HF (0.15-0.80Hz) LF (0.03-0.15Hz)	cycle; NA; max incremental	HF ↓ (with ↑ int); LF ↓ (with ↑ int); LF:HF ↔ (with ↑ int)
Bernardi et al. (1990)	HF (0.15-0.80Hz) LF (0.05-0.12Hz) TP (0.00-0.80Hz)	cycle; NA; max incremental	HF:TP ↓ (with ↑ int); HF:TP ↑ at max; LF:TP ↑ (with ↑ int); LF:TP ↓ at max

HF = high-frequency power
LF = low-frequency power
NA = not applicable
TP = total power
int = intensity
max = maximal
↑ = increase
↓ = decrease
↔ = no change
bpm = beats per minute
T_{vent} = ventilatory threshold
VO_{2max} = maximal oxygen consumption
rpm = revolutions per minute
min = minute
nu = normalized units

Table Con'd.

Table A.4

Author/Date	Frequencies analyzed	Exercise (mode; duration; intensity)	Results
Brenner et al. (1993)	HF (0.15-0.80Hz) LF (0.06-0.15Hz)	supine cycle; 8 min; 100 & 150 bpm	HF ↓ at 100 & 150 bpm; LF ↓ at 100 & 150 bpm
Hayashi et al. (1992)	HF (0.15-0.50Hz) LF (0.00-0.15Hz)	cycle; NA; 20% & 100% T_{vent}	HF ↔ at 20%; HF ↓ at 100%; LF:HF ↔ at 20%; LF:HF ↑ at 100%
Kamath et al. (1991)	HF (0.18-0.40Hz) LF (0.08-0.11Hz)	cycle; 10 min; 50% VO_{2max}	HF ↓ vs. supine rest; HF ↔ vs. stand rest; LF ↑ vs. supine rest; LF ↔ vs. stand rest
Perini et al. (1990)	HF (0.15-1.0Hz) LF (0.05-0.15Hz) TP (0.0-1.0Hz)	cycle; 5 min; 21%, 49%, & 70% VO_{2max}	HF ↓ at 21%, 49%, & 70%; HF:TP ↔ at 21%, 49%, & 70%; LF:TP ↔ at 21%, ↓ at 49% & 70%; LF:HF ↓ at 21%, 49%, & 70%
Perini et al. (1993)	HF (0.15-1.0Hz) LF (0.05-0.15Hz) TP (0.0-1.0Hz)	cycle; 6 min; 14%, 28%, 45%, & 67% VO_{2max}	HF:TP ↑ at 14% & 28%; HF:TP ↓ at 45% & 67%; LF:TP ↔ at 14% & 28%; LF:TP ↓ at 45% & 67%

Table Con'd.

Table A.4

Author/Date	Frequencies analyzed	Exercise (mode; duration; intensity)	Results
Perini et al. (1998)	HF (0.15-1.0Hz) LF (0.04-0.15Hz)	cycle; 6 min; 0, 50, 125, & 175 W at 60rpm	HFnu ↓ with ↑ intensity LFnu ↑ with ↑ intensity
Sekiguchi et al. (1979)	HF (0.25-0.30Hz) LF (0.10Hz)	Treadmill; 10 min; moderate & max	HF ↓ at moderate & max LF ↓ at moderate & max
Sun et al. (1993)	HF (0.15-1.0Hz) LF (0.05-0.15Hz) TP (0.0-1.0Hz)	supine cycle; 14 min; 30% peak work rate	HF ↓; HF:TP ↔; LF ↓; LF:TP ↔
Yamamoto et al. (1991)	HF (0.15-1.0Hz) LF (0.05-0.15Hz)	cycle; 17 min; 20 watts, 30%, 60%, 90%, 100%, & 110% T_{vent}	HF progressively ↓ at all workloads; LF:HF ↔ at 20 watts, 30%, 60%, 90%, & 100% T_{vent}; LF:HF ↑ at 110% T_{vent}
Warren et al. (1997)	HF (0.15-0.1Hz) LF (0.05-0.15Hz)	cycle; 6 min; 0, 50, 100, 150 W	HF ↓ with ↑ intensity LF:HF ↔ with ↑ intensity

Research further suggests that power in the LF range of the HR spectrum is also reduced during rhythmic exercise (Arai et al. 1989; Perini et al. 1993; Sekiguchi et al. 1979; Sun et al. 1993). Although both HF and LF power are decreased with acute exercise, one would expect the balance of sympathetic to parasympathetic activity, expressed as either LF:HF or as normalized units, to be altered to reflect an increased sympathovagal balance. Indeed, several studies have supported this hypothesis. For example, Nakamura, Yamamoto, and Murakoa (1993), Yamamoto et al. (1991), and Hayashi, Nakamura, and Murakoa (1992) reported increases in the LF:HF ratio at submaximal workloads, while Perini et al. (1998) reported increases and decreases in LF and HF normalized units, respectively, with increasing exercise intensity. In contrast, Arai et al. (1989) and Warren et al. (1997) reported no change in LF:HF with increasing exercise intensity, while Perini et al. (1990) reported decreases in LF:HF at an intensity of 70% VO_{2max}.

Rowell and O'Leary (1990) reported that vagal withdrawal appears to be nearly complete at exercise heart rates of approximately 100 beats • minute $^{-1}$ in humans. At intensities greater than this, sympathetic nervous activity begins to rise as indicated by increases in MSNA, plasma NE and plasma rennin, and decreases in renal and splanchnic blood flow (Christensen & Brandsborg, 1973; Rowell & O'Leary, 1990). Pharmacological studies have further supported these findings and have similarly reported an early decrease in parasympathetic activity during moderate exercise, and a gradual increase in sympathetic activity at intensities that elicit heart rates greater than 100 beats • minute $^{-1}$ (Ekblom, Goldbarg, Kilbom, & Astrand, 1972; Fagraeus & Linnarsson, 1976; Maciel, Gallo, Marin Neto, Lima Filho, & Martins, 1986; Robinson, Epstein, Beiser, & Braunwald, 1966). Hohimer, Hales, Rowell, and Smith (1983) reported an increased blood flow to the heart and

exercising skeletal muscle, while blood flow was reduced to the skin, splanchnic organs, kidneys, nonexercising skeletal muscle, and subcutaneous adipose tissue during mild cycling exercise, suggesting a significant sympathetic response.

The withdrawal of vagal efferent activity at the onset on exercise is believed to be primarily mediated by central command (Williamson, Nobrega, Winchester, Zim, & Mitchell, 1995). Signals arising from a central area of the brain activate the motor cortex and the CVC in the medulla, which, in turn, alters autonomic outflow via a feedforward mechanism (Mitchell, 1990). Although some researchers have also hypothesized a role of muscle mechanoreceptors in mediating this autonomic alteration (Hollander, & Bouman, 1975), it appears that central command plays a predominant role at exercise onset. For example, Williamson et al. (1995) recently demonstrated that the RR interval can be shortened within 300 ms of voluntary cycling, which is quicker than the time-course needed for muscle mechanoreceptors (~550 ms), providing evidence for a predominant role of central command at the onset of exercise. However, as exercise time increases, various autonomic reflex play a role in regulating CV function.

Contracting skeletal muscle during rhythmic exercise activates both mechanically and chemically sensitive muscle afferents that reflexly activate the CVC in the medulla. This reflex, commonly referred to as the "exercise pressor reflex," therefore results in autonomic alterations and plays a major role in the CV response to rhythmic exercise. As previously mentioned, Hollander and Bouman (1975) provided evidence supporting the muscle-heart reflex in which the activation of mechanically sensitive muscle afferents can initiate a vagal withdrawal (independent of central command) within 550 ms.

O'Leary (1993) provided evidence for a significant role of muscle metaboreceptors in regulating the CV response to exercise. By using post-exercise muscle ischemia with or without atropine or propranolol, he demonstrated that both the HR and BP responses to exercise are mediated, at least in part, by sympathetic outflow to the heart via activation of the muscle chemoreflex. He further reported that during parasympathetic blockade, the reduction in HR following exercise was attenuated, suggesting that increases in vagal activity can obscure the influence of the muscle metaboreflex on the heart.

As described previously, the baroreceptors act as a negative feedback controller and are important to the beat-to-beat regulation of BP at rest. However, the transition from rest to exercise is marked by an increase in both HR and BP. Obviously this could only occur if the baroreflex is somehow altered by the exercise. There is a general consensus that the arterial baroreflex is reset to a higher operating pressure at the onset of rhythmic exercise, without a concurrent change in sensitivity (Bevegard, & Shepard, 1966; Melcher, & Donald, 1981; Potts, Shi, & Raven, 1993). Using bilateral carotid occlusion, Melcher and Donald (1981) demonstrated that the HR and BP stimulus-response curves were the same at rest and during exercise indicating no difference in BRS between conditions. Their study also demonstrated that the removal of extracarotid baroreceptor input by vagotomy yielded no difference in carotid baroreceptor sensitivity during exercise. Using varying amounts of neck pressure/suction, Potts et al. (1993) constructed stimulus-response curves of the baroreflex during rest and exercise at 25% and 50% VO_{2max}. They demonstrated that the open-loop stimulus-response relationship of the carotid baroreflex is reset during dynamic exercise by shifting the baroreflex response curve to new systemic pressures. They also reported that the operating-point of the baroreflex curve was shifted away from the centering point towards the

threshold region. Therefore, at rest the carotid baroreflex can alter cardiac and vascular responses to both increases and decreases in BP, whereas during exercise it responds more readily to a hypertensive stimulus. This likely enables the receptors to respond better to the hypertensive response of exercise resulting from the exercise pressor reflex. Ludbrook and Graham (1985) further reported that the resetting of the baroreflex operating point occurs faster than the change in BP, resulting in a baroreflex error signal. Such an error signal may cause an overshoot in HR at the onset of exercise, but as exercise time progresses, the BP increases closer to the operating point and HR is reduced slightly to a lower steady-state value. For the most part, the aortic baroreceptors function in concert with the carotid baroreceptors. The primary differences between the two are that baroreceptors of the aortic arch work at higher operating pressures (Raven, Potts, & Shi, 1997) and account for one-third more of the entire arterial baroreflex than the carotid baroreceptors (Sanders, Ferguson, & Mark, 1988).

The cardiopulmonary baroreceptors also play an important role in the regulation of BP during rhythmic exercise. These receptors, which are sensitive to cardiac filling volume and central venous pressure, regulate BP by peripheral vasoconstriction or vasodilation (Raven et al. 1997). As previously mentioned, Melcher and Donald (1981) provided evidence for a significant role of the cardiopulmonary baroreceptors during exercise by assisting the carotid baroreflex in establishing the operating range. Furthermore, Mack, Nose, and Nadel (1988) concluded that during exercise the cardiopulmonary baroreflex is involved in regulating cardiac filling pressure and is reset to higher cardiac filling pressures to regulate the increased cardiac filling volumes during exercise. Potts, Shi, and Raven (1995) also reported that exercise combined with –18 torr of lower body negative pressure (unloading of

cardiopulmonary baroreceptors) results in an augmented carotid baroreceptor gain suggesting that the cadiopulmonary baroreceptors exert a tonic inhibition on the carotid baroreflex during exercise. Although the exact mechanism by which the baroreflex is reset during rhythmic exercise has not been elucidated, both central command and activation of muscle afferents are believed to play a role.

In conclusion, at the onset of an acute bout of rhythmic exercise, there is a withdrawal of parasympathetic activity to the heart. This withdrawal is likely mediated via central command, although the role of the arterial baroreflex cannot be dismissed. As exercise intensity increases, there is a gradual sympathetic activation, which may be mediated via muscle mechanoreceptors, muscle metaboreceptors, and/or the arterial baroreflex (via further resetting).

Mitigating Factors of Autonomic Regulation

Age. There are many changes in cardiovascular function that are associated with age that implicate age-related changes in ANS activity. Several of these changes can be attributed to alterations in autonomic nervous system activity. However, while CV regulation differs between old and young individuals, the effects of age versus the effects of factors that may co-vary or interact with age (e.g. lifestyle, physical fitness, nutritional status, disease, etc.), have not been completely elucidated. Thus, one must exercise caution when describing differences between the young and old, as age usually does not account for all of the variance in the data.

As individuals grow older, maximal HR is reduced, while resting and maximal SBP are elevated. The resting end-diastolic volume index (end-diastolic volume normalized for body size) and stroke volume index increase with age, while end-diastolic and end-systolic

volume indices are greater in older versus younger individuals during maximal exercise. While cardiac ejection fraction and cardiac index at rest appears to be unaffected by age, they are dramatically reduced in older individuals during maximal or near-maximal exercise. Additionally, peripheral vascular resistance increases with age at rest and during maximal exercise. (Fleg et al. 1990).

As previously mentioned, cardiac output has been reported to be influenced by age. Furthermore, each of the factors that determine cardiac output (heart rate, preload, afterload, coronary flow, myocardial cell performance) is subject to autonomic modulation. An age-related reduction in the effectiveness of sympathetic modulation of the cardiovascular response to exercise could contribute to some of these alterations. For example, it has been reported that the age-related changes in the end-diastolic volume index and end-systolic volume index during upright cycle exercise do not occur in the presence of propranolol (Fleg et al. 1991). Conway, Wheeler, & Sannerstedt (1971) further demonstrated that the age-related decrease in cardiac index during exercise is reduced under β-blockade.

It seems unlikely that the age-associated reduction in the effectiveness of β-adrenergic modulation of the cardiovascular system during exercise is caused by a reduced secretion of catecholamines during exercise. Numerous reports have demonstrated that resting plasma concentrations of NE and E are greater in older subjects, reflecting an increased spillover into the plasma (Featherstone et al. 1987; Fleg, Tzankoff, & Lakatta, 1985; Goldstein et al. 1983; Pfeifer et al. 1983; Prinz, Halter, Benedetti, & Raskind, 1979; Rowe & Troen, 1980; Rubin, Scott, McLean, & Reid, 1982; Sowers, Rubenstein, & Stern, 1983). A more likely explanation for age-associated reductions in adrenergic modulation is that responses to β-adrenergic stimulation decline with age. That is, neurotransmitters are not as effective at the

level of the target organ (Lakatta, 1993). For example, it has been demonstrated that isoproterenol infusion elicits a greater increase in left ventricular ejection fraction and cardiac index in young compared to older subjects (Stratton et al. 1992). Infusions of β-adrenergic agonists (Kuramoto, Matsushita, Mifune, Sakai, & Murakami, 1978; London, Safar, Weiss, & Milliez, 1976; Stratton et al., 1992; Vestal, Wood, & Shand, 1979; Yin, Spurgeon, Greene, Lakatta, & Weisfeldt, 1979) and isoproterenol (Abrass, Davis, & Scarpace, 1982; Le Blanc & Rakusan, 1987; O'Conner, Scarpace, & Abrass, 1981) result in a reduced heart rate response with increasing age. Although these results could be explained by either a reduced response to adrenergic stimuli or by increased vagal modulation of the heart with advancing age, Yin et al. (1979) demonstrated that the heart rate increase in response to isoproterenol infusion in the presence of vagal blockade decreases with age.

Although, early evidence for changes in vagal modulation with increasing age were not entirely clear, more recent evidence suggests a reduction in parasympathetic activity with age. For example, Chevalier, Mansier, Teiger, Callens-El Amrani, & Swynghedauw (1991) reported that the number of cholinergic receptors in the left ventricle, along with the response to acetylcholine decreased with age. Additionally, numerous studies have demonstrated that HRV and BRS decrease with age (Laitinen et al. 1998; O'Mahony, Bennett, Green, & Sinclair, 2000; Schwartz, Gibb, & Tran, 1991; Shannon, Carley, & Benson, 1987; Waddington, MacCulloch, & Sambrooks, 1979).

Researchers have also addressed the effects of age on vascular responsiveness to adrenergic stimuli. Pan, Hoffman, Pershe, & Blaschke (1986) demonstrated that the redistribution of blood to skeletal muscle and various other organs during isoproterenol infusion decreases with age. Using a dog model, Yin, Weisfeldt, & Milnor (1981) reported a

reduced β-adrenergic relaxant effect on aortic smooth muscle. Additionally, Van Brummelen, Buhler, Kiowski, & Amann, (1981) showed a reduced dilation of forearm vasculature in response to isoproterenol infusion with age.

Race. Several studies have suggested racial differences in autonomic activity. For example, African American children have been shown to exhibit a more pronounced alpha-adrenergic increase in peripheral vasoconstriction than Caucasians (Treiber, Musante, Braden, et al., 1990). Additionally, borderline hypertensive Caucasian adults have a higher increase in cardiac index (Sherwood, Hinderliter, & Light, 1995), while their African American counterparts exhibit a higher increase in vascular tone (Sherwood, May, Siegal, & Blumenthal, 1995). Furthermore, Caucasian children reportedly exhibit higher HR and CO at rest (Voors, Webber, & Berenson, 1980), while African American children exhibit greater peripheral vascular resistance (Soto, Kikuchi, Arcilla, Savage, & Berenson, 1989). Other studies have demonstrated reduced plasma renin levels in African Americans compared to Caucasians, suggesting a lower sympathetic tone (Gillum, 1979; He, Klag, Appel, Charleston, & Whelton, 1999).

Regarding studies that have used HRV, Liao, Barnes, Chambless, Simpson, Sorlie, & Heiss (1995) reported that African Americans exhibited favorable HRV parameters (higher HF, lower LF, and lower LF/HF) compared to Caucasians in a large population study. Furthermore, Urbina, Bao, Pickoff, and Berenson (1998) demonstrated greater pNN50 values and lower LF/HF for African Americans compared to Caucasians during supine rest and during several CV reactivity tests. In contrast, by controlling for environmental factors (i.e. diet, alcohol consumption, physical activity), Horodyski, De Meersman, Vandenburgh, and Gallagher (1995) reported that there were no racial differences in HRV and BRS. However,

the subjects of this study were cadets at a military academy and the high volume of physical training in which they were involved may have overshadowed any racial differences that were present.

The findings of He et al. (1999), Voors et al. (1980), Liao et al. (1995), and Urbina et al. (1998) suggest increased sympathetic activity in Caucasians and increased parasympathetic modulation in African Americans. This has puzzled investigators since previous studies have reported a sympathetic predominance in early hypertension (Pieper, & Hammill, 1995; Takalo, Korhonen, Turjanmaa, Majahalme, Tuomisto, & Uusitalo, 1994) and there is a higher prevalence of hypertension in the African American population (Hypertension Detection and Follow-up Program Cooperative Group, 1979). Although there is no clear explanation for these findings, it may be that the lower sympathetic activity in African Americans is a consequence of an elevated plasma volume of renal origin (Gillum, 1979; Schachter, & Kuller, 1984).

Gender. There are several studies that suggest a significant effect of gender on autonomic balance in young adults. For example, Hirsch and Bishop (1981) reported a trend towards higher RSA in a group of 7 females compared to that of 10 age-matched males. Ryan, Goldberger, Pincus, Mietus, and Lipsitz (1994) reported a greater total and HF spectral power of HRV in young women compared to a group of age-matched males. Additionally, Gregoire et al. (1994) reported a greater HF-to-TP ratio and a lower LF-to-HF ratio, which would suggest a lower sympathovagal balance, in females (age=21.6±2 yr) compared to males (age=21.4±1 yr) of similar fitness levels. In a recent study in healthy adults (age=20-83 yr), Barnett et al. (1999) reported that females exhibited a lower NE response to head-up tilt, and an elevated HF power of HRV at rest, compared to age-matched healthy males. Other recent

studies have provided similar results (Huikuri et al. 1996; Rossy & Thayer, 1998). Furthermore, Matsukawa, Sugiyama, Watanabe, Kobayashi, and Mano (1999) recently reported that MSNA was significantly lower in a group of women under 50 years of age compared to age-matched males.

In contrast, studies seem to suggest that no gender differences in autonomic balance exist in older subjects. For example, in a cohort of 15,800 subjects (age=45-64 yr), Liao et al. (1995) reported no differences in HF power between males and females. Furthermore, they reported a higher LF/HF in females, which contradicts the majority of the findings in younger subjects. Ryan et al. (1994) also reported that the gender-related differences in HRV present in younger adults, are not present in middle-aged and older adults. Additionally, in a previously mentioned study (Matsukawa et al. 1999), there were no differences in resting MSNA in subjects greater than 50 years of age.

Thus, research seems to suggest that in young adults, females may exhibit a lower sympathovagal balance compared to males of similar health status. However, in older adults, the age-related increase in sympathetic drive appears to negate these gender differences. A possible mechanism for the differences in autonomic control between males and females is hormonal levels. Specifically, estrogen and progesterone, which are significantly higher in young females have been reported to alter sympathetic autonomic outflow. For example, it has been reported that infusions of estrogen reduce the NE response to mental stress in postmenopausal women (Del Rio et al. 1994), and also that progesterone infusion reduces plasma NE in men (Tollan, Oina, Kjelden, Eida, & Maltass, 1993). This would therefore explain why gender differences were no longer present in older adults. In conclusion, there is

evidence that gender is a significant factor that may influence autonomic modulation and should be considered in research investigations.

Environment. Several environmental factors, including temperature and altitude, influence autonomic regulation and, therefore, should be considered when investigating autonomic function. For example, there is ample evidence to suggest that elevated environmental temperatures result in an augmented sympathetic outflow. Several studies that have used HRV as an index of autonomic control have reported attenuated HF power, suggesting a reduction in vagal outflow to the heart and/or an enhanced sympathetic outflow (Brenner, Thomas, & Shepard, 1997; Parsons, Scott, & Macdonald, 1992; Saul, 1990). In rats, Walsh (1969) reported similarly that infusion of either atropine or a beta-antagonist blocked the rise in HR associated with an increase in core temperature from 35 to 40 degrees Celsius. Likewise, Gorman and Proppe (1984) reported that infusions of atropine or propranolol attenuated the HR rise to arterial temperature increases of 2-3 degrees Celsius. Furthermore, they estimated that the autonomic contributions of the sympathetic and parasympathetic branches to the temperature-induced HR elevation were 15% and 45%, respectively. Additionally, Niimi et al. (1997) reported an elevated MSNA during temperature increases from 29 to 40 degrees Celsius. Together, these studies suggest that increases in environmental temperature lead to an elevated sympathetic noradrenergic outflow, likely in order to redistribute blood towards the skin to facilitate body cooling via convection.

Acute periods of cold stress also elicit elevations in sympathetic activity. In fact, researchers have used the cold pressor test, which involves a subject immersing a limb in cold water, as an index of CV reactivity for a number of years. Some of the CV responses to acute periods of cold stress include increases in ventilation, HR, BP and TPR, and a reduced blood

flow to the periphery as blood is shunted towards the core of the body (Brooks, Fahey, & White, 1995). Furthermore, Kinugasa and Hirayanagi (1999) recently reported a decreased HF component of the power spectrum of HRV along with an increase in LF/HF in response to acute cold stress (18 degrees Celsius), reflecting a reduced parasympathetic and/or increased sympathetic cardiac outflow. Thus it appears that acute exposure to a cold environment results in alterations in autonomic balance favoring an enhanced sympathetic noradrenergic component.

Another environmental condition that may substantially influence autonomic nervous system activity is altitude-induced hypoxia. Hypoxic conditions not only effect ventilation (via chemoreceptors in the aortic and carotid bodies), but also influence autonomic CV regulation by activating the sympathoadrenal system. For example, several researchers have reported that acute exposure to high altitude ($\geq$4000 meters) results in the elevation of arterial and urinary catecholamines **(**Mazzeo et al. 1991; Mazzeo, Wolfel, Butterfield, & Reeves, 1994; Pace, Grinswold, & Grunbaum, 1964; Surks, Beckwitt, & Chidsey, 1967). These sympathoadrenal responses, therefore, can influence CV variables including HR, BP, and vascular resistance. In fact, by using autonomic blockade via propranolol and atropine, Koller, Drechsel, Hess, Macherel, & Boutellier (1988) reported that increases in HR, BP and CO induced by exposure to simulated altitude (6000 meters) were mediated by both an elevated sympathetic and a reduced parasympathetic activity. Studies that have used HRV to assess the autonomic response to hypoxic environments have also provided evidence to support these findings. For example, Hughson, Yamamoto, McCullough, Sutton, and Reeves (1994) reported that following 4-5 days at 4300 m, there were alterations in spectral power to reflect an increased sympathetic and reduced parasympathetic influence on the heart. They

also reported a slight recovery towards pre-hypoxic values for these indices following 11-12 days at altitude. Ponchia et al. (1994) further reported a reduction in cardiac vagal modulation, noted by attenuated HF power and pNN50, following 1 week of exposure to an altitude of 5000 meters. Lastly, Bernardi et al. (1998) recently reported that acute (1 day) exposure to altitude (4970 meters) resulted in reduced HF and elevated LF spectral power, also reflecting a reduced vagal modulation of the heart. In closing, these findings suggest that acute hypoxia results in an elevated sympathetic drive with a concomitant reduction of parasympathetic outflow, both of which may alter CV variables.

Influence of Peak Aerobic Power on Autonomic Regulation of the Cardiovascular System

Aerobic fitness, as defined by peak aerobic power, is related to autonomic regulation of the CV system. Compared to individuals of a low-to moderate fitness level, high-fit subjects have been shown to exhibit significant alterations in certain CV variables (i.e. reduced resting HR, reduced resting BP, increased CO). Interestingly, there is evidence that several of the alterations in these variables may be the result of fitness-related differences in autonomic nervous system activity. Therefore, the purpose of this section of the review is to examine cross-sectional studies that have used various methodologies to look at the relationship between aerobic fitness and autonomic regulation of the CV system.

Studies assessing CV reactivity to laboratory stressors. Research regarding the influence of aerobic fitness on CV reactivity to laboratory stressors has produced equivocal results. Several studies have reported improvements in CV reactivity in subjects with enhanced fitness (Boutcher, Nugent, McLaren, & Weltman, 1998; Claytor, Cox, Howley, Lawler, & Lawler, 1988; Czajkowski et al., 1990; De Geus, Van Doornen, De Visser, & Orlebeke, 1990; Holmes & McGilley, 1987; Holmes & Roth, 1985; Hull, Young, & Ziegler, 1984; Lake,

Suarez, Schneiderman, & Tocci, 1985; Light, Obrist, James, & Strogatz, 1987; McCubbin, Cheung, Montgomery, Bulbulian, & Wilson, 1992; Perkins, Dubbert, Martin, Faulstich, & Harris, 1986; Shulhan, Scher, & Furedy, 1986; Sothmann, Horn, Hart, & Gustafson, 1987; Spalding, Jeffers, Porges, & Hatfield, 2000; Turner, Carroll, Costello, & Sims, 1988; Van Doornen & De Geus, 1989), while others have reported no differences (Dorheim, Ruddel, & Eliot, 1984; Plante, & Karpowitz, 1987; Sinyor, Golden, Steinert, & Seraganian, 1986), and even exaggerated responses (De Geus, Van Doornen, & Orlebeke, 1993). A list of studies examining this relationship can be seen in Table 5.1. The majority of studies have reported reduced CV reactivity to stress in subjects with a higher aerobic capacity. For example, in a population of young subjects (age=18-26 yr), Van Doornen and De Geus (1989) examined CV reactivity to a reaction time task and reported that those with higher fitness (n=8; VO_{2max} =67.2 ml•kg^{-1}•min^{-1}) demonstrated lower HR, SV, DBP, TPR, and cardiac pre-ejection period (PEP) reactivity than those with lower aerobic fitness (n=7; VO_{2max} =48.9 ml•kg^{-1}•min^{-1}). By assessing CV reactivity to video games and mental arithmetic, Perkins et al. reported that hypertensives that had undergone 10-weeks of exercise training (n=11; age=44±10 yr) exhibited less BP reactivity compared to their untrained counterparts (n=7; age=47.4±11 yr), while no differences in HR reactivity were noted. McCubbin et al. reported less HR reactivity to a mental arithmetic task in high- (n=14; age=23±1 yr; VO_{2max}=44.7±1 ml•kg^{-1}•min^{-1}) compared to low-fit (n=14; age=20±1 yr; VO_{2max}=36.6±1 ml•kg^{-1}•min^{-1}) individuals, while no differences were noted in BP reactivity. Furthermore, they suggested that differences in HR reactivity were mediated via an opioid neuropeptide mechanism, as group differences were not significant under the opioid-blocking drug naloxone. Lake et al. provided evidence suggesting that while HR reactivity is not different in subjects with varying fitness levels

Table A.5

Cross-Sectional Studies evaluating the effect of Aerobic Power on Cardiovascular Reactivity to Stress.

Author/Date	Stressor	Dep.Var.	Findings
Boutcher et al. (1998)	Stroop CWCT	HRV	↑ decrease in HRV in fit & unfit w/ low resting HRs
Brooke & Long (1987)	Rapelling	HR, E, NE, cortiisol	Faster recovery of E
Claytor et al. (1988)	Reaction time	HR, BP, E, NE	↓ HR reactivity in high-fit
Czajkowski (1990)	M.A., Video game	HR, BP	↓ HR & BP reactivity in high-fit
De Geus et al. (1990)	Tone avoidance	HR, BP, TPR RSA, PEP, CO, SV	↓ DBP, MAP, RSA reactivity in fit
De Geus et al. (1993)	Reaction time	HR, BP, PEP, CO, TPR	↑ BP reactivity in fit subjects
Dorheim et al. (1984)	Reaction time	HR, BP	No differences
Hollander et al. (1984)	Word recognition	HR, Skin conductance	Faster HR recovery in fit subjects

HR = heart rate
HRV = heart rate variability
BP = arterial pressure
SBP = systolic blood pressure
DBP = diastolic blood pressure
CO = cardiac output
SC = skin conductance
RR = RR interval
CWCT = color word conflict task
↑ = increase
M.A. = mental arithmetic
E = epinephrine
NE = norepinephrine
TPR = total peripheral resistance
SV = stroke volume
PEP = pre-ejection period
VO_2 = oxygen consumption
RSA = respiratory sinus arrhythmia
↓ = decrease
Dep. Var. = dependent variable

Table Con'd.

Table A.5

Author/Date	Stressor	Dep.Var.	Findings
Holmes & McGilley (1987)	M.A.	HR	↓ HR reactivity in fit subjects
Holmes & Roth (1985)	M.A.	HR, BP	↓ HR reactivity in fit subjects
Hull et al. (1984)	Stroop CWCT	HR, BP, NE	↓ DBP reactivity in fit subjects
Keller & Seraganian (1984)	Stroop CWCT	HR, SC	Faster HR recovery in fit subjects
Lake et al. (1985)	M.A. Card games	HR, BP	↓ BP reactivity during M.A.; ↑ BP reactivity during games in fit
Light et al. (1987)	Reaction time	HR, BP, PEP	↓ HR, SBP, & PEP reactivity in active
McCubbin et al. (1992)	M.A.	HR, BP	↓ HR reactivity in fit
Perkins et al. (1986)	M.A. Video games	HR, BP	↓ BP reactivity in fit
Plante et al. (1987)	I.Q. test	HR	No difference
Shulhan et al. (1986)	M.A.	HR, T-wave on EKG	↓ T-wave in fit
Sinyor et al. (1983)	Stroop CWCT M.A. EKG quiz	HR, E, NE, prolactin, cortisol	Faster HR recovery & peak NE
Sinyor et al. (1986)	M.A., Tone avoidance	HR, BP	No difference

Table Con'd.

Table A.5

Author/Date	Stressor	Dep.Var.	Findings
Sothmann et al. (1987)	Stroop CWCT	E, NE	↓ NE reactivity in fit
Spalding et al. (2000)	M.A. Stroop CWCT	RR, RSA	↑ RR during stress in fit
Steptoe et al. (1990)	Problem solving	HR, BP, RR, SC	↓ RR & faster HR recovery in fit
Szabo et al. (1994)	M.A.	HR, BP	Faster HR recovery in fit
Turner et al. (1988)	M.A.	HR, BP, VO_2	↓ HR reactivity in fit
Van Doornen &. De Geus (1989)	Reaction time	HR, BP, TPR SV, CO, PEP	↓ HR, SV, PEP, DBP, & TPR reactivity in fit

(*n*=40; age=19 yr; VO_{2max}=54.2-67.7 ml•kg^{-1}•min^{-1} vs. *n*=21; age=19; VO_{2max}=37.4-47.6 ml•kg^{-1}•min^{-1}), BP reactivity during mental arithmetic is significantly lower in high-fit subjects. However, they further noted that BP reactivity was actually greater in the high-fit individuals during competitive card games. This seemingly contradictory finding was suggested not to be a result of different aerobic capacity, but explained by the fact that the high-fit individuals were competitive athletes and were possibly better able to increase noradrenergic outflow during competition than the lower fit subjects. Using both treadmill time to exhaustion and self-reported physical activity, Hull et al. reported that DBP reactivity to the Stroop CWCT was attenuated in fit (*n*=9; age=30±2 yr) relative to unfit (*n*=16; age=41±4 yr) subjects. Although there were no group differences in HR, SBP, NE, or E reactivity to the stressor, the investigators failed to take group differences in age into account

when performing these analyses, which may have confounded the results. Additionally, their method of assessing physical fitness was not ideal, thus differences in fitness may have possibly been exaggerated. Holmes and Roth (1985) demonstrated a reduced HR response to the backwards digit counting test of the Weschler Adult Intelligence Scale in undergraduate women with a mean VO_{2max} of 53.5 ml•kg^{-1}•min^{-1} (*n*=10) compared to those with a mean VO_{2max} of 28.8 ml•kg^{-1}•min^{-1} (*n*=10). However, this group used a submaximal cycle ergometer test to estimate VO_{2max}, so it is therefore possible that the subjects' fitness level was not accurately represented. Sothmann et al. reported group differences in catecholamine reactivity to the Stroop CWCT in high- (*n*=10; age=39±3 yr; VO_{2max}=65.4±6 ml•kg^{-1}•min^{-1}) compared to low-fit (*n*=9; age=42±4; VO_{2max}=44.6±4 ml•kg^{-1}•min^{-1}) individuals. Specifically, they found that plasma NE reactivity was significantly attenuated in the high-fit group, although there were no group differences in HR and E reactivity. Holmes and McGilley (1987) were able to show fitness-related differences in the HR response to mental arithmetic, as subjects classified as highly fit (*n*=34; age=17-20 yr) exhibited a lower response to the stressor compared to a group classified as low-fit (*n*=34; age=17-20 yr). However, it is possible that true differences in fitness were not present, as functional capacity was evaluated via a questionnaires and the 12 minute walk/run test. De Geus et al. demonstrated a significant negative correlation between the BP response to a tone avoidance task and a positive correlation between VO_{2max} and vagal withdrawal, measured by the respiratory sinus arrhythmia (RSA), in response to a memory task and the tone avoidance task in 24 healthy individuals (age=18-28 yr; VO_{2max}=46.4±5 ml•kg^{-1}•min^{-1}). However, they were unable to show any relationship between fitness and CV reactivity to the cold pressor test. Additionally, no significant relationships were found between fitness and the reactivity of

other CV variables [HR, cardiac PEP, respiratory rate (RR), CO, SV, & TPR]. Boutcher et al. used HRV to quantify fitness-related differences in the vagal response to stress. By assessing a group of trained runners (*n*=10; age=21±1 yr; $VO_{2max=}$75.4±1 ml•kg^{-1}•min^{-1}), a group of untrained subjects with low resting HRs (*n*=10; age=22±4 yr; VO_{2max}=58.8±1 ml•kg^{-1}•min^{-1}), and a group of untrained subjects with high resting HRs (*n*=10; age=22±1 yr; VO_{2max}=51.4±1 ml•kg^{-1}•min^{-1}), they reported significantly greater reductions in HRV for the trained and low HR groups compared to the high HR group in response to both mental arithmetic and the Stroop CWCT. From these results, they suggested that both fitness and genetic influences play a role in the CV response to stress. Steptoe et al. demonstrated lower RR reactivity and a tendency towards lower HR reactivity (*p*=0.06) to a problem-solving task in moderately-fit (n=40; age=39±11 yr; VO_{2max}=40.2±8 ml•kg^{-1}•min^{-1}) compared to unfit (n=35; age=39±11 yr; VO_{2max}=29.1±7 ml•kg^{-1}•min^{-1}) subjects. However, no fitness-related differences were identified for BP or skin conductance reactivity, although HR recovery was quicker in the fit. Using age as a covariate, Czajkowski et al. reported reduced HR, SBP, and DBP reactivity to a video game task in high-fit (*n*=32; mean age=41 yr) compared to lesser-fit subjects (*n*=30; mean age=30 yr), with fitness classification based on time to exhaustion during a treadmill test. However, there were no group differences in CV reactivity to mental arithmetic. Shulhan et al. examined the effect of aerobic fitness on the T-wave on an ECG in response to a mental arithmetic task. They reported a greater T-wave attenuation in low- (*n*=12; mean age=24.7 yr; mean VO_{2max}=44.0 ml•kg^{-1}•min^{-1}) as compared to high-fit (*n*=12; mean age=25.8 yr; mean VO_{2max}=54 ml•kg^{-1}•min^{-1}) subjects suggesting a fitness-related reduction of cardiac sympathetic activity. However, the use of T-wave amplitude as an index of cardiac sympathetic activity remains controversial (Furedy & Heslegrave, 1983) and they found no

group differences in HR reactivity. Moreover, this study used a submaximal step test to predict VO_{2max} leading to possible misclassification of some subjects into high- or low-fit categories. Additionally, Brooke and Long (1987) reported no fitness-related differences were found regarding CV reactivity to a rapelling task in "fit" (*n*=9; age=25±2 yr; VO_{2max}=58±4 ml•kg^{-1}•min^{-1}) compared to "unfit" subjects (*n*=9; age=27±4 yr; VO_{2max}=48±4 ml•kg^{-1}•min^{-1}). However, the lack of group differences in this study could possibly be a result of how fitness was classified, as the "unfit" group exhibited an average VO_{2max} of 48 ml•kg^{-1}•min^{-1} which can hardly be considered unfit.

There is also some evidence to suggest that enhanced aerobic fitness is associated with an improved recovery of CV variables following a stressor (Brooke & Long, 1987; Hollander & Seraganian, 1984; Keller & Seraganian, 1984; Sinyor, Schwartz, Peronnet, Brisson, & Seraganian, 1983; Szabo et al, 1994; Steptoe, Moses, Mathews, & Edwards, 1990). For example, Brooke and Long reported that their "fit" subjects exhibited a faster recovery of E to baseline values following a rapelling task compared to those that were "unfit". They hypothesized that the enhanced E recovery may be the result of a protective sympatho-inhibitory effect in the fit subjects. However, there were no group differences in HR or NE recovery. Similarly, Szabo et al. reported a faster HR recovery following a mental arithmetic task in subjects with a higher (*n*=10; age=16±1 yr; VO_{2max}=64.3±4 ml•kg^{-1}•min^{-1}) compared to a lower aerobic capacity (*n*=10; age=16±1 yr; VO_{2max}=52.7±4 ml•kg^{-1}•min^{-1}), although no group differences were reported for CV reactivity. Again, this group's failure to find group differences in HR or BP reactivity could be a result of their classification of fitness, as the lower group exhibited an average VO_{2max} of 52 ml•kg^{-1}•min^{-1}. Sinyor et al. further demonstrated a more rapid HR recovery following the Stroop CWCT in highly trained

individuals (n=15; VO_{2max}=69 ml•kg^{-1}•min^{-1}) compared to those who were untrained (n=15; VO_{2max}=33 ml•kg^{-1}•min^{-1}). Furthermore, this group reported a delayed onset of NE to stress in untrained subjects.

In a recent study, Spalding et al. (2000) reported that individuals with a higher level of aerobic fitness (n=10; age=24±1 yr; VO_{2max}=67.0±2 ml•kg^{-1}•min^{-1}) exhibited a greater heart period at rest, during psychological stress, and during recovery than lower fit (n=10; age=22±1 yr; VO_{2max}=45.4±2 ml•kg^{-1}•min^{-1}) counterparts. However, they found no group differences in cardiac vagal tone, as assessed by RSA, during rest or stress. Subsequently, this group concluded that the group differences in heart period were not vagally-mediated and could possibly be a result of differences in sympathetic influences, differences in intrinsic heart rate, and/or genetic influences. This study is unique in that it controlled for the Law of Initial Values (Wilder, 1957), which states that group differences in baseline values of a variable may influence the magnitude of change of that variable. By using Myrtek and Foerster's (1986) procedure, they were able to conclude that heart period responses were not dependent on baseline values. Therefore, the use of analysis of covariance (ANCOVA) or regression techniques to account for initial group differences would have been inappropriate in this study as it may have also been inappropriate in a number of previous studies. However, a limitation to this study was their small number of subjects.

As one may surmise, research is ambiguous regarding the influence of aerobic fitness on the CV response to stress. Methodological and analytical differences between studies make it hard to draw clear-cut conclusions. Some of the reasons for the discrepancies in the data could be a result of statistical modeling, the technique by which aerobic fitness was evaluated, the different classifications of fitness level, and/or subject selection. For example,

several earlier studies did not test for the presence of the LIV (Holmes & McGilley, 1987; Holmes & Roth, 1985; Lake et al., 1985; Light et al., 1987; Plante et al., 1987; Sothmann et al., 1987) and may have used ANCOVA or regression analyses inappropriately. Furthermore, a few studies ignored initial group differences and may have failed to adjust their statistical modeling in the presence of the LIV (Boutcher et al., 1998; Brooke & Long, 1987; Hull et al., 1984). As previously eluded to, studies have used a variety of techniques to measure aerobic fitness. Obviously, the best estimate of aerobic fitness would be a direct VO_{2peak} obtained from a maximal graded exercise test. However, several of the studies have used other methods such as submaximal tests (Holmes & Roth, 1985; Holmes & McGilley, 1987), time to exhaustion (Czajkowski et al., 1990), and even self-report techniques (Claytor et al., 1988). Additionally, it is difficult to compare the results of studies that have used different classifications of high-fit and low-fit individuals (Szabo et al., 1994; Brooke & Long, 1987). Furthermore, discrepancies between studies could be a result of subject selection. For example, after Czajkowski et al. (1990) controlled for angry temperament, the group differences in DBP reactivity were no longer significant. Also, studies comparing competitive athletes to sedentary subjects could potentially mask fitness-related differences in CV reactivity as athletes most likely have a different psychological make-up than sedentary individuals (Dorheim et al., 1984). In conclusion, there is evidence both for and against an influence of CV fitness on CV reactivity to laboratory stressors. Thus, it is of benefit to also examine this relationship using other methodologies.

Studies assessing plasma catecholamines. Cross-sectional studies that have searched for a relationship between resting catecholamine concentrations and aerobic fitness have failed to provide evidence to support this hypothesis. For example, Shi et al. (1992) reported no

difference in resting plasma NE (0.25±0.07 vs. 0.36±0.09 ng•ml^{-1}) between high- (*n*=6; age=28±2 yr; VO_{2max}=61.7±2 ml•kg^{-1}•min^{-1}) and low-fit (*n*=6; age=26±1 yr; VO_{2max}=38.4±2 ml•kg^{-1}•min^{-1}) young, adult males. Convertino et al. (1993) also compared high- (*n*=6; age=30±1 yr; VO_{2max}=54.8±1 ml•kg^{-1}•min^{-1}) and low-fit (*n*=6; age=32±1 yr; VO_{2max}=40.5±1 ml•kg^{-1}•min^{-1}) groups and found no difference in resting NE (2.3±0.3 vs. 2.2±0.2 pmol•ml^{-1}, respectively) or E (0.28±0.06 vs. 0.34±0.1 pmol•ml^{-1}, respectively). Additionally, Van Faassen et al. (1992) and Oleshansky, Zoltick, Herman, Mougey, & Meyerhoff (1990) both reported no relationship between aerobic fitness, as estimated by VO_{2max} (*n*=45; age=22±3 yr; VO_{2max}=55±10 ml•kg^{-1}•min^{-1}) and treadmill time to exhaustion, (*n*=17; age=39.8±10 yr; 15.2±0.7 min), and resting plasma NE or E. Poehlman, McAuliffe, & Danforth (1990) further examined NE kinetics in active (*n*=21; age=24±5 yr) and inactive (*n*=20; age=27±6 yr) young, and active (*n*=11; age=66±4 yr) and inactive (*n*=15; age=68±5 yr) older men, with VO_{2max}'s of 66.0±5, 57.3±5, 51.1±6, and 37.9±4 ml•kg fat-free weight^{-1}•min^{-1}, respectively. Interestingly, they reported that the active older subjects exhibited greater levels of resting plasma NE relative to the other 3 groups. Additionally, when adjusted for fat-free mass and body surface area, the older active adults displayed greater rates of NE appearance, while activity level had little effect on the NE clearance rate. Although these investigators did not run statistical tests to look specifically at plasma NE kinetics between young active and inactive subjects, the data appear to suggest that the NE appearance rate was lower in the active relative to the inactive young subjects, although there did not appear to be group differences in plasma NE concentration nor in the NE clearance rate. Kjaer et al. (1984) also reported no difference in plasma NE between trained (*n*=8; VO_{2max}=65±4 ml•kg^{-1}•min^{-1}) and untrained (*n*=7; VO_{2max}=49±4 ml•kg^{-1}•min^{-1}) subjects. However, resting plasma E was

elevated in the trained group (0.30±0.06 vs. 0.09±0.03 nmol•l^{-1}). These findings have also been extended to females, as Armstrong (1998) was unable to find any group differences in resting plasma NE between trained (*n*=5; age=28±1 yr; VO_{2max}=56.7±4 ml•kg^{-1}•min^{-1}) and untrained (*n*=5; age=28±6 yr; VO_{2max}=35.0±1 ml•kg^{-1}•min^{-1}) women. Additionally, several other investigations have also reported no effect of physical fitness on resting catecholamines (Braun, Potempa, Holm, Fogg, & Szidon, 1994; Hagberg et al. 1988; Kjaer, Christensen, Sonne, Richter, & Galbo, 1985; Lehmann, Dickhuth, Schmid, Porzig, & Keul, 1984; Lehmann & Keul, 1986; Lehmann, Schmid, & Keul, 1984).

Although it appears that fitness has little influence on resting plasma catecholamines, it may be more appropriate to examine catecholamines under stressful conditions (physical or psychological) during which there is less inter-individual variability. Accordingly, studies have also evaluated the relationship between aerobic fitness and the catecholamine response to physiological perturbations (i.e. exercise, tilt, psychological challenges, etc.). However, in order to maintain a concise review, only those involving dynamic exercise and psychological stress will be reviewed. Investigations evaluating the relationship between fitness and the catecholamine response to dynamic exercise have been somewhat conclusive in that most have reported that subjects of lower fitness levels exhibit an exaggerated NE response to a given (absolute) level of submaximal exercise. However, the E response remains debatable (Braun et al. 1994; Hagberg et al. 1988; Kjaer et al. 1985; Lehmann, Dickhuth, et al. 1984; Lehmann & Keul, 1986; Lehmann, Schmid et al. 1984). For example, Lehmann, Dickhuth et al. found no differences in resting plasma NE (2.64 vs. 2.17 nmol•l^{-1}) or E (1.01 vs. 0.57 nmol•l^{-1}) between endurance trained (*n*=6; age=32±5 yr; VO_{2max}=65.7±2 ml•kg^{-1}•min^{-1}) and non-endurance trained (*n*=6; age=27±2 yr; VO_{2max}=54.0±3 ml•kg^{-1}•min^{-1}) individuals. They

also reported a reduced NE response during treadmill running at 12 and 14 km•hr^{-1} in their trained versus untrained subjects, although there were no group differences at maximal exercise. They further reported an increased beta-receptor density in the athletes (2150 vs. 1300 receptors), estimated by ^{3}H-Dihydroalprenolol binding to leukocytes. However, close examination of these data suggests that the non-trained group was, in fact, physically conditioned, suggesting that fitness-related differences in the NE response to exercise may be present even at high-fitness levels. In a subsequent, but poorly described investigation, Lehmann, Schmid et al. reported no difference in resting NE or E between a group of trained cyclists (*n*=9; age=26±3 yr) and untrained healthy subjects (*n*=10; age=28±3 yr). Additionally, they reported that the cyclists exhibited lower plasma concentrations of NE and E at identical submaximal workloads, although group differences were not present at maximal effort. In yet another investigation, Lehmann and coworkers (Lehmann & Keul) reported no differences in resting plasma NE (3.89±1.6 vs. 2.48±0.7 nmol•l^{-1}) or E (0.60±0.2 vs. 0.41±0.2 nmol•l^{-1}) between trained cyclists (*n*=10; age=25±3 yr; VO_{2max}= 65.8±5 ml•kg^{-1}•min^{-1}) and untrained subjects (*n*=9; age=27±3 yr; VO_{2max}=46.7±9 ml•kg^{-1}•min^{-1}). They further reported significantly higher NE and E at cycling workloads of 100, 150, 200, and 250 watts in their untrained subjects compared to the cyclists, whereas there were no group differences at maximal intensity. Hagberg et al. examined the catecholamine response to 60 minutes of treadmill exercise at 70% VO_{2max} in groups of young (*n*=11; age=25±5 yr; VO_{2max}=64.9±5 ml•kg^{-1}•min^{-1}) and older (*n*=11; age=65±4 yr; VO_{2max}=50.0±5 ml•kg^{-1}•min^{-1}) trained and young (*n*=13; age=26±3 yr; VO_{2max}=46.4±4 ml•kg^{-1}•min^{-1}) and older (*n*=10; age=65±4 yr; VO_{2max}=26.8±2 ml•kg^{-1}•min^{-1}) untrained subjects. There were no notable group differences in plasma E at rest or during exercise. Plasma NE, however, was significantly higher in the

older untrained subjects at rest, whereas the older trained men displayed resting NE levels similar to younger subjects. Additionally, plasma NE was significantly higher at 30 and 60 minutes of exercise in the young trained subjects compared to the other three groups, leading to increased lipolysis. Similarly, the older trained subjects exhibited a greater NE response to exercise than the older untrained group. Kjaer et al. looked specifically at E kinetics during exercise in athletes (*n*=6; age=21-26 yr; ±4 yr; VO_{2max}=59-83 ml•kg^{-1}•min^{-1}) and sedentary (*n*=6; age=20-25 yr; VO_{2max}=39-49 ml•kg^{-1}•min^{-1}) controls. They assessed plasma E at rest and during incremental cycling to exhaustion, and subsequently calculated the clearance and appearance rates. There were no differences in E clearance at rest between groups, although resting plasma concentration (1.42±0.27 vs. 0.71±0.16 nmol•l^{-1}) and appearance (2.9±0.7 vs. 1.5±0.4 nmol•min^{-1}) were significantly greater in the athletes. Plasma E was not different between groups at workloads of 125 and 160 watts, but was substantially greater in the athletes at maximal intensity. The dramatic rise in plasma E in the athletes was more than could be accounted for by clearance alone, which was strongly related to relative workload and initially increased, and then decreased at intensities greater than 30% VO_{2max}. With regard to NE, there were no group differences at rest, although they reported a greater plasma NE response to submaximal exercise in the control group. Additionally, the athletes displayed significantly greater NE concentrations at maximal workloads. Lastly, Braun et al. demonstrated no relationship between VO_{2max} and resting NE or E in a group of hypertensive subjects (*n*=27; age=45±12 yr; VO_{2max}=30.9±10 ml•kg^{-1}•min^{-1}). Furthermore, they found an inverse relationship between VO_{2max} and plasma NE (*r*= -0.44) during cycle ergometry at 100 Watts, while reporting positive relationships between VO_{2max} and NE and E (*r*= 0.73 and 0.6, respectively) during maximal exercise.

Studies assessing the plasma catecholamine response to a psychological challenge have provided equivocal results with some reporting fitness-related differences and others reporting no differences. For example, Brooke and Long (1987) reported no differences between subjects with a VO_{2max} ~48 ml•kg^{-1}•min^{-1} and those with a VO_{2max} of ~58 ml•kg^{-1}•min^{-1} with regards to NE or E reactivity to rapelling. However, they noted a more efficient recovery of plasma E in the subjects with higher aerobic fitness levels. Similarly, Claytor et al. (1988) found differences between high- (VO_{2max} ~71 ml•kg^{-1}•min^{-1}) and low-fit (VO_{2max} ~45 ml•kg^{-1}•min^{-1})subjects in NE or E reactivity to a reaction time and the cold pressor test. Using groups of similar aerobic fitness levels (VO_{2max} ~71 ml•kg^{-1}•min^{-1} vs. VO_{2max} ~47 ml•kg^{-1}•min^{-1}) Hull et al. (1984) further reported no group differences in NE of E reactivity to the Stroop color word task or the cold pressor test. De Geus et al. (1993) also reported no relationship between VO_{2max} and NE or E reactivity to the cold pressor and reaction-time tasks in a group of untrained subjects. On the other hand, Sothmann et al. (1987) reported that low-fit individuals (VO_{2max} ~32 ml•kg^{-1}•min^{-1}) exhibited an elevated NE response to the Stroop test compared to high-fit individuals (VO_{2max} ~51 ml•kg^{-1}•min^{-1}), although no group differences in E reactivity were noted. Additionally, Sinyor et al. (1983) reported a delayed onset of the NE response to a cognitive task in low-fit (VO_{2max} ~33 ml•kg^{-1}•min^{-1}) compared to high-fit (VO_{2max} ~69 ml•kg^{-1}•min^{-1}) subjects, while no group differences in E were reported.

Taken as a whole, research seems to indicate that fitness is not associated with plasma catecholamines at rest, although a few studies have reported greater resting E in high-fit subjects (Kjaer et al. 1984; Kjaer et al. 1985). It also appears that there is a reduced plasma NE response to exercise at the same absolute intensity in high- compared to low-fit subjects,

whereas the E response is more variable. This could possibly be explained by an increased sensitivity or up-regulation of adrenergic receptors leading to a reduced catecholamine secretion. However, at the same relative workload (%VO_{2max}), the data of Hagberg et al. (1988) suggest that high-fit subjects may exhibit a greater catecholamine response. Hagberg et al. proposed that this assisted in increasing the rate of lipolysis in trained subjects. Furthermore, at maximal intensity exercise, it appears that both NE and E are greater in high- compared to low-fit subjects. This last finding is likely a reflection of the higher workloads that high-fit subjects are able to obtain, although Kjaer et al. (1985) proposed a training-induced increased responsiveness of the adrenal medulla. With regards to the catecholamine response to psychological challenges, the studies that found no fitness-related differences in NE reactivity compared groups with VO_{2max}s of ~58-70 ml•kg^{-1}•min^{-1} and 45-48 ml•kg^{-1}•min^{-1}, which is actually comparing "high-fit" subjects to "moderately-fit" subjects. Conversely, the studies that did find fitness-related differences used lower-fit groups with VO_{2max}s of ~32-33 ml•kg^{-1}•min^{-1}, which more accurately represents a "low" fitness level. It is therefore possible that the apparent fitness-related differences in these studies are the result of some physiological phenomenon associated physical deconditioning (i.e. body composition, blood pressure). Another conclusion that can be drawn from this data is that there is no relationship between fitness and E reactivity, as none of the studies found any group differences.

Studies assessing the variability of heart rate and blood pressure. In healthy adults, several studies have evaluated the relationship between aerobic fitness and HRV or the respiratory sinus arrhythmia (RSA; the maximum range or the standard deviation of RR interval sequence) with most showing a positive relationship (Bonaduce et al. 1998; Boutcher et al. 1998; De Meersman, 1993; Dixon, Kamath, McCartney, & Fallen, 1992; Gallagher, Terenzi,

& De Meersman, 1992; Goldsmith, Bigger, Bloomfield, & Steinman, 1997; Goldsmith, Bigger, Steinman, & Fleiss, 1992; Gregoire, Tuck, Yamamoto, & Hughson, 1996; Janssen, de Bie, Swenne, & Oudhof, 1993; Kenney, 1985; Shin, Haruyuki, Onishi, Yamazaki, & Lee, 1997; Sloan et al. 1997). For example, Kenney reported that aerobic power was significantly correlated with the variation in heart period. In a group of healthy adults (age=29±8; VO_{2max}= 41-80 ml•min^{-1}•kg^{-1}), Kenney found a correlation coefficient of 0.92 between VO_{2max} and HRV, expressed as the difference between the maximal and minimal RR intervals within a 7 beat cycle. However, one methodological problem of this study was that the subjects synchronized their breathing with HR. Therefore, these results may have been slightly biased as subjects of a greater fitness level exhibited lower resting HRs. Similarly, De Meersman reported a significant augmentation of HRV, expressed as the percent change from the mean heart rate, in runners compared to sedentary individuals. The runners exhibited significantly higher values of VO_{2max} compared to their sedentary counterparts of the same age group (15-25, 26-35, 36-45, 46-55, 56-65, and >65 years) and HRV was higher in runners of all age groups, although the difference did not reach significance in the 36-45 yr and the > 65 yr groups. De Meersman concluded that habitual aerobic activity augments HRV and counteracts the age-related HRV reduction. Gallagher et al. reported significantly augmented vagal modulation of the heart in a group of high-fit (age= 38±8 yr; VO_{2max}= 70±5 ml•min^{-1}•kg^{-1}) compared to sedentary (age= 43±10 yr; VO_{2max}= 29±7 ml•min^{-1}•kg^{-1}) subjects. The high-fit group exhibited a LF/HF of 0.288 compared to that of 0.315 in the sedentary group. Dixon et al. compared a group of male long distance runners (age=28.4±4 yr) and a group of sedentary males (age=27.4±3 yr) and reported significantly elevated HF and lower LF power in the runners supporting the hypothesis that physical fitness is related to sympathovagal

balance. Goldsmith et al. (1992) reported differences in HRV measured over a 24-hour between 8 endurance-trained men (age=28±4 yr; VO_{2max}= 67±5 ml•min^{-1}•kg^{-1}) and 8 age-matched controls (age=29±3 yr; VO_{2max}=35±5 ml•min^{-1}•kg^{-1}). In this study, SDNN, TP LF, and TP were significantly greater in the endurance-trained men. Janssen et al. found differences in autonomic balance as assessed by HRV between a group of professional cyclists (age=19-32 yr) and a group of nonathletes (age=23-33 yr). In this study, the cyclists exhibited greater pNN50 and lower LF power, expressed as normalized units, compared to the nonathletes in the supine position. However, they failed to show any group differences in pNN50 and LF power in the standing position. Additionally, the cyclists exhibited higher, although not significantly different, values of SDNN in both the supine and standing positions. With this data it was concluded that the athletes exhibited greater parasympathetic and/or a lower sympathetic modulation of the heart in the supine, but not the standing position. Sloan et al. also reported a significant positive relationship between VO_{2max} and LF (r=0.48) and HF (r=0.41) power of the HR power spectrum in a group of subjects aged 19-36 years. Shin et al. compared athletes (age=22±2 yr; VO_{2max} >55 ml•min^{-1}•kg^{-1}) and nonathletes (age=21±1 yr; VO_{2max} <45 ml•min^{-1}•kg^{-1}) with respect to spectral measures of HRV. They reported significantly higher HF normalized units in the athletes. Additionally, while group differences for LF power did not reach statistical significance, there was a tendency for LF power to be reduced in the athletes (p=0.07) suggesting a reduced sympathetic cardiac modulation. However, Shin et al. reported no group differences in spectral indices of SBP or DBP variability. From this data it was concluded that higher aerobic fitness is associated with a parasympathetic dominance, which contributes to the resting bradycardia seen in athletes. Furthermore, in a population of young adults (age=20-25

yr), Boutcher et al. reported significantly higher spectral indices of HRV in the HF and LF ranges in subjects with a VO_{2max} of ~75 ml•min^{-1}•kg^{-1}compared to those with a VO_{2max} of ~51 ml•min^{-1}•kg^{-1}. In a group of adults (age=22-44 yr; VO_{2max}=25-70 ml•min^{-1}•kg^{-1}), Goldsmith et al. (1997) reported a significant relationship between VO_{2max} and HF power of the HRV spectrum. This study found no relationship between HF power and age and concluded that the reported age-associated reduction in vagal modulation may actually be due to an age-related decline in fitness. Bonaduce et al. further reported elevated HRV in a group of cyclists (age=21±4 yr; VO_{2max}=62±4 ml•min^{-1}•kg^{-1}) compared to sedentary controls (age=21±3 yr; VO_{2max}=43±4 ml•min^{-1}•kg^{-1}). They reported elevated SDNN, pNN50, rMSSD, TP, LF, and HF, along with a lower LF/HF in the cyclists. In an additional study, Gregoire et al. compared subjects of different fitness levels, age, and gender. These investigators reported that middle-aged subjects, who had a history of exercising aerobically at least 5 times a week for >45 minutes, exhibited lower LF/HF, higher HF/TP (an index of vagal activity), and a trend towards higher SDNN (p=0.08). However, they were unable to find differences in HRV between trained (age=27±4 yr; VO_{2max}=59±5 ml•min^{-1}•kg^{-1}) and untrained (age=21±2 yr; VO_{2max}=49±6 ml•min^{-1}•kg^{-1}) young subjects.

Conversely, Reilling and Seals (1988) reported no significant relation between HRV and physical fitness. This study compared 12 collegiate cross-country athletes (age=20$\pm$1 yr) to 12 untrained college students (age=22$\pm$1 yr). Although the athletes exhibited significantly lower resting HRs, there were no group differences in SDNN. From these data, they concluded that the resting bradycardia seen in athletes was of non-autonomic origin. However, the failure of Reilling and Seals to measure spectral indices of HRV may have played a role in their lack of finding group differences. Additionally, Sacknoff, Gleim,

Stachenfeld, and Coplan (1994) reported that a group of athletes (age=26±2 yr) exhibited lower spectral indices of HRV (TP, LF, and HF) compared to untrained controls (age=30±1 yr), although time domain parameters (SDNN and pNN50) were greater in the athletes as predicted. From these data, Sacknoff et al. concluded that spectral indices of HRV may not be sensitive to detecting differences in fitness levels. However, it should be noted that these investigators used self-report measures of physical activity and resting HR as indicators of fitness. Therefore, these subjects may have not actually been significantly different with regards to fitness level.

Similar findings have been demonstrated in older adults. For example, Yataco, Fleisher, and Katzel (1997) demonstrated that senior athletes (age=69±7 yr; VO_{2max}=41±6 $ml \cdot min^{-1} \cdot kg^{-1}$) exhibited greater HRV indices than sedentary individuals of a similar age (age=69±4 yr; VO_{2max}=24±2 $ml \cdot min^{-1} \cdot kg^{-1}$). All parameters of HRV measured (SDNN, rMSSD, LF, LH, TP, and LF/HF) were significantly greater in the athletes suggesting a greater parasympathetic modulation of the heart. Additionally, Van den Hombergh, Dekker, and Schouten (1995) used regression analysis to report a positive association between SDNN in the supine position and the scores on a physical activity questionnaire in a group of men aged 65-85. However, this association was not present in older women of the same age, nor was it present in the standing position. These studies suggest that aerobic fitness is positively associated with parasympathetic modulation of the heart. Most studies have reported that HF power, which reflects cardiac vagal activity, is significantly elevated in subjects of a high fitness level when resting in a supine position. This enhanced vagal modulation of the heart likely contributes to the resting bradycardia seen in high-level athletes.

Studies assessing baroreflex sensitivity. Studies that have assessed the influence of aerobic fitness on BRS have provided mixed results. In young, adult males, there have been several reports of an attenuation of baroreflex control of HR in endurance-trained athletes, resulting in orthostatic intolerance (Luft, Myrhe, Leoppky, & Venters, 1976; Mack, Shi, Nose, Tripathi, & Nadel, 1987; Raven, Rohm-Young, & Blomqvist; 1984; Shi, Andresen, et al., 1993; Shi, Crandall, et al., 1993; Smith et al. 2000; Smith, Graitzer, Hudson, & Raven, 1988). By using LBNP to selectively unload the cardiopulmonary baroreceptors, Luft et al. reported a decreased tolerance (527 Torr/min vs. 913 Torr/min) and an increased incidence of presyncopal reactions in a group of athletes (VO_{2max}= 50 ml•kg^{-1}•min^{-1}) compared to nonathletes (VO_{2max}= 34 ml•kg^{-1}•min^{-1}). They further reported a higher rate of change of leg volume per unit Torr and time of exposure for the athletes (0.75% 100 Torr^{-1}•min^{-1} vs. 0.42% 100 Torr^{-1}•min^{-1}), suggesting an increased venous compliance or possibly a less effective vasoconstrictor response in the athletes. Raven et al. reported a lower tachycardic response and lower peripheral resistance in a group of endurance athletes (age=27±2 yr; VO_{2max}= 70.2±3 ml•kg^{-1}•min^{-1}) compared to subjects of an average fitness level (age=28±2 yr; VO_{2max}= 41.3±3 ml•kg^{-1}•min^{-1}) in response to graded LBNP. However, there were no group differences in leg venous compliance. Similarly, Mack et al. found differences in BRS between fit and unfit subjects using LBNP to unload the baroreceptors. This group reported a diminished gain of the baroreceptors, expressed as the relationship between forearm vascular resistance and estimated central venous pressure, in "fit" subjects (age= 31±2 yr; VO_{2max}= 54±2 ml•kg^{-1}•min^{-1}) compared to "unfit" subjects (age= 30±3 yr; VO_{2max}= 38.5±3 ml•kg^{-1}•min^{-1}). They reported baroreflex gains, expressed as the slope of vascular resistance-peripheral vascular pressure, of –2.42 units/mmHg and –5.15 units/mmHg for fit and unfit

subjects, respectively. They further reported a significantly higher blood volume in the fit group and noted a linear relationship between blood volume and baroreflex gain, suggesting that blood volume could possibly play a role in the lower BRS in trained subjects.

Since LBNF elicits both hypotension and central hypovolemia, this technique likely results in an integrated response of the arterial and cardiopulmonary baroreceptors. Therefore, researchers have used other techniques in an attempt to distinguish between the two. Smith et al. (1988) used both LBNP and phenylephrine (PE) infusion to examine fitness-related differences in cardiopulmonary and arterial BRS, using the PE method specifically to examine the arterial baroreceptors. The data of Smith et al. during LBNP supported previous findings as they reported an attenuated BRS, calculated by ΔHR/ΔSBP (0.91±0.3 vs. 1.62±0.3 bpm•mmHg^{-1}) and ΔHR/ΔMAP (2.05±0.3 vs. 4.08±0.4 bpm•mmHg^{-1}), in the endurance-trained group (*n*=10; age=25±2 yr; VO_{2max}= 65.0±1 ml•kg^{-1}•min^{-1}) compared to the untrained group (*n*=10; age=27±1 yr; VO_{2max}= 42.8±1 ml•kg^{-1}•min^{-1}). Furthermore, they found an attenuated BRS, expressed as the slope of HR against SBP during PE infusion in the trained subjects (-0.57 vs. –0.91) although the difference was not as great as during LBNP. The data from this investigation further provided evidence that BRS is attenuated in "trained" subjects and that this difference is mediated by a combination of arterial and cardiopulmonary baroreceptors.

Shi, Andresen et al. (1993) proposed that the aortic baroreflex may be more sensitive to change than the carotid baroreflex and, with an elegant experimental design, estimated the relative influences of the carotid and aortic baroreceptors in average-fit (*n*=7; age=27.9±2 yr; VO_{2max}= 42.9±1 ml•kg^{-1}•min^{-1}) and high-fit subjects (*n*=7; age=26.4±2 yr; VO_{2max}= 62.3±2 ml•kg^{-1}•min^{-1}). This group calculated BRS, expressed as ΔHR/ΔMAP, during PE infusion,

which is believed to stimulate both the carotid and aortic baroreceptors, and during PE infusion combined with neck pressure (NP) and/or LBNP, which is believed to isolate the aortic baroreflex. They then calculated the carotid BRS by subtracting the aortic ratios (PE + NP and PE + NP + LBNP) from the total arterial BRS obtained during PE infusion alone. They reported that the total arterial BRS was attenuated in the high- compared to the average-fit subjects (0.33±0.04 vs. 0.94±0.14). They further reported a reduced aortic BRS in the high- compared to the average-fit subjects (0.16±0.02 and 0.14±0.03 bpm/mmHg vs. 0.52±0.08 and 0.59±0.08 bpm/mmHg, for PE + NP and PE + NP + LBNP respectively). Additionally, they reported no difference in carotid BRS, estimated by BRS during PE infusion alone minus BRS during PE + NP + LBNP, between the high- (0.19±0.02 bpm/mmHg) and average-fit groups (0.35±0.09 bpm/mmHg). Furthermore, they reported between group differences in the relative contribution of the carotid BRS to the total arterial BRS, with it contributing 35% in the average-fit group compared to 59% in the high-fit group. With these data, Shi et al. concluded that the sensitivity of the aortic baroreflex control of HR was reduced in the high-fit subjects and that the aortic baroreflex predominantly contributes to the HR reflex control in average-fit subjects, while in high-fit subjects the carotid baroreflex predominates. Furthermore, it was concluded that the attenuated arterial BRS in high-fit subjects is due mainly to alterations in aortic BRS. In a follow-up study, Shi, Crandall et al. (1993) compared the isolated aortic baroreflex between high (*n*=7; age=26±1 yr; VO_{2max}=64±2 ml•kg^{-1}•min^{-1}) and average fit (*n*=8; age=28±1 yr; VO_{2max}=45±1 ml•kg^{-1}•min^{-1}) subjects. After infusing sodium nitroprusside to induce a drop in BP, they used calculated neck and lower body positive pressures in an attempt to remove the influences of the carotid and cardiopulmonary baroreceptors, respectively. They reported that aortic BRS was

significantly attenuated in the high-fit group, as they exhibited lower HR responses to the induced drop in BP (+7.9±2 bpm) compared to the average-fit subjects (+16.8±3 bpm) and had significantly lower baroreceptor gains (1.0±0.3 vs. 1.9±0.3 bpm•mmHg^{-1}). Similar to the previous study, they also reported that the percent contribution of the aortic to the total arterial baroreflex was significantly higher in average- compared to high-fit subjects. Most recently, Smith et al. (2000) also reported a reduced arterial BRS in high-fit subjects (*n*=8; age=24±1 yr; VO_{2max}= 61.9±2ml•kg^{-1}•min^{-1}) relative to their average-fit counterparts (*n*=8; age=25±1 yr; VO_{2max}= 42.2±2 ml•kg^{-1}•min^{-1}). Using techniques similar to Shi, Crandall et al. (1993), they were able to construct stimulus-response curves of the arterial, aortic, and carotid baroreflexes in each group. With this data, they reported an attenuated arterial and aortic BRS in the high-fit group, while carotid BRS remained similar between groups. They further noted a vertical downward shift of the arterial and aortic baroreflex curves in the high-fit individuals as a result of a smaller HR response range, without a difference in the operating point (resting MAP).

Other investigators have reported either no effect of fitness (Fiocchi, Fagard, Vanhees, Grauwels, & Amery, 1985; Levine et al. 1991; Shin et al. 1997; Williamson & Raven, 1994) or an augmented BRS (Barney et al. 1988; Savard & Lundie, 1994) in individuals with a high fitness level. Fiocchi et al. were unable to find a significant relationship between physical fitness and carotid BRS, expressed as the slope of the linear relationship between RR interval response and various degrees of neck suction. However, they studied touring cyclists with a narrow range of fitness levels, all of whom could be classified as being highly fit (*n*=47; age= 33±1 yr; VO_{2max}= 54±1 ml•kg^{-1}•min^{-1}). Similarly, Levine et al. reported no differences in carotid BRS between high- (*n*=8; age= 25±2 yr; VO_{2max}= 60±1 ml•kg^{-1}•min^{-1}), mid- (*n*=8;

age= 23±1 yr; VO_{2max}= 49±1 ml•kg^{-1}•min^{-1}), and low-fit (*n*=8; age= 24±1 yr; VO_{2max}= 36±1 ml•kg^{-1}•min^{-1}) subjects. Using varying levels of neck suction/pressure, Levine et al. found no differences in carotid BRS assessed by either open-loop gain [acute (~10 second) changes in RR interval or BP in response to varying neck pressure] or closed-loop gain [steady-state (2-min) changes in BP in response to varying neck pressure]. Despite similar carotid BRS among groups, they did report that the high-fit subjects exhibited a reduced tolerance to LBNP. With this data, Levine et al. concluded that the orthostatic intolerance in highly fit athletes may be a result of differences in cardiovascular variables, such as vascular conductance and stroke volume, that interact with baroreceptor function. Although, another possible mechanism might be an exclusive reduction in sensitivity of the aortic baroreflex. Williamson and Raven specifically sought to determine if the carotid baroreflex differed between 8 high- (age=26.7±3 yr; VO_{2max}=64.5±2ml•kg^{-1}•min^{-1}) and 8 low-fit (age=28.3±3 yr; VO_{2max}=39.8±4ml•kg^{-1}•min^{-1}) subjects, and further investigated whether there was a difference between the gains of the right and left sided carotid baroreflex. They evaluated the RR interval response to various levels of neck suction/pressure, applied both unilaterally and bilaterally. They then reported that there were no group differences in the gains of the right (5.3±1 vs. 4.5±1 ms•mmHg^{-1}), left (3.3±1 vs. 3.6±2 ms•mmHg^{-1}), and combined (6.4±2 vs. 5.9±1 ms•mmHg^{-1}) carotid baroreceptors. Shin et al. also found no difference between high- (*n*=15; age=21.5±1 yr; VO_{2max}= 61.3±4 ml•kg^{-1}•min^{-1}) and low-fit (*n*=15; age=22.1±2 yr; VO_{2max}= 40.3±2 ml•kg^{-1}•min^{-1}) subjects in regards to BRS estimated by the cross-spectral technique. In this study, the cross-spectrum of SBP and RR variations in the low and high frequency ranges were not significantly different between groups. Shin et al. proposed that a possible reason for their findings was that the cross-spectral technique does not allow for a

differentiation between the carotid, aortic, and cardiopulmonary baroreceptors. On the other hand, Barney et al. reported an enhanced responsiveness of the carotid baroreflex in high-fit subjects (*n*=11; age=24.3±1 yr; VO_{2max}= 60.4±1 ml•kg^{-1}•min^{-1}) compared to sedentary controls (*n*=9; age=24.0±1 yr; VO_{2max}= 39.3±2 ml•kg^{-1}•min^{-1}). In this study, the high-fit subjects exhibited a significantly greater increase RR interval in response to –40 mmHg and –20 mmHg of neck pressure, and also displayed a greater, although not statistically significant, decrease in RR interval in response to 35 mmHg. Additionally, this group reported an augmented BRS, expressed as the slope derived by the change in RR interval to each neck pressure, in the high-fit compared to the sedentary group (4.0±0.4 vs. 2.5±0.3 ms/mmHg). Furthermore, they reported a significant positive relationship between VO_{2max} and the carotid baroreflex slope (*r*=0.48). With these data, Barney et al. concluded that the responsiveness of the carotid baroreflex is maintained in high-fit individuals, possibly as a result of augmented vagal outflow and/or enhanced cardiac responsiveness to vagal outflow. Similarly, Savard and Lundie (1994) reported that the carotid baroreflex was significantly enhanced in a group of endurance-trained (*n*=7; VO_{2max} >55ml•kg^{-1}•min^{-1}) compared to a group of sedentary subjects (*n*=8; VO_{2max} <48 ml•kg^{-1}•min^{-1}). In this study, the trained individuals demonstrated a greater maximal gain of the carotid baroreflex (9.3±5 ms•mmHg^{-1}) relative to the sedentary subjects (4.3±3 ms•mmHg^{-1}) in response to various levels of neck suction/pressure,

In contrast to the numerous studies that have evaluated the relationship between BRS and physical fitness in healthy, young adult males, only a few studies have specifically looked at this relationship in healthy, young females. Hudson, Smith, and Raven (1987) evaluated this relationship in trained (*n*=8; age=23.0±3 yr; VO_{2max}= 56.8±1 ml•kg^{-1}•min^{-1}) and untrained (*n*=8; age=25.9±2 yr; VO_{2max}= 39.4±2 ml•kg^{-1}•min^{-1}) females using incremental

LBNP (0 to –50 torr). In this study, no differences were noted in BRS, estimated by ΔHR/ΔSBP, between groups. However, they did report that at –50 torr the trained subjects did not further enhance vasoconstriction, suggesting that fitness-related differences may have been present beyond –50 torr. Additionally, Davy, Desouza, Jones, and Seals (1998) examined BRS by the sequence technique in sedentary (*n*=23; age=28±1 yr; VO_{2max}= 35.3±1 ml•kg^{-1}•min^{-1}) and physically active (*n*=22; age=31±1 yr; VO_{2max}= 52.5±1 ml•kg^{-1}•min^{-1}) females. In this investigation they reported significantly higher BRS in the physically active group (19±3 bpm/mmHg) compared to the sedentary subjects (11±2 bpm/mmHg). Furthermore, Davy et al. examined this relationship in older females and found similar results with the physically active females displaying a higher BRS than their sedentary counterparts (13±2 vs. 7±2 bpm/mmHg).

In addition to Davy et al. (1998), a few other studies have also examined this relationship in older adults and reported similar findings. For example, Fortney et al. (1992) compared the CV responses of 9 trained (age=63.9±2 yr; VO_{2max}= 52.4±2 ml•kg^{-1}•min^{-1}) and 9 untrained (age=65.6±2 yr; VO_{2max}= 31.0±3 ml•kg^{-1}•min^{-1}) older adults to graded LBNP. In this study, the investigators reported that the trained individuals were better able to maintain cardiac output and MAP during LBNP, and exhibited smaller decreases in stroke volume, end-systolic volume, and end-diastolic volume. Additionally, two of the nontrained subjects could not complete the entire LBNP protocol due to the presence of presyncopal symptoms. With these data, they concluded that aerobic fitness is associated with improved orthostatic responses in older adults. Bowman et al. (1997a) reported similar findings while using the α–index to compare BRS between a group of sedentary older adults (*n*=26; age=67±5 yr) and a group of older half-marathon runners (*n*=8; age=66±2 yr). These investigators reported a

significantly higher HF component of the α–index in the runners compared to the sedentary individuals. From these data, they concluded that the age-associated reduction in BRS is attenuated by endurance exercise training in older adults.

Taken as a whole, a few conclusions can be drawn from these studies. Those investigations that have specifically examined the aortic baroreflex, clearly have demonstrated an attenuated BRS in exercise-trained individuals. On the other hand, it appears that the carotid baroreflex is not significantly different between subjects of various fitness levels. Additionally, the effect of fitness on the cardiopulmonary baroreceptors remains unclear. Some of the proposed mechanisms that may play a role in mediating BRS differences between high-fit and average-fit individuals include differences in blood volume and autonomic balance. Together, the chronic expansion of total blood volume and increase in cardiac vagal modulation seen in endurance trained subjects will increase resting stroke volume by increasing cardiac preload and prolonging cardiac filling. Consequently, there will be an increased stretch on the aortic baroreceptors, which may result in adaptation or down-regulation. Another possible mechanism is that the increased central blood volume in high-fit subjects may elicit afferent impulses from the cardiopulmonary baroreceptors, which has been shown to have an inhibitory effect on the arterial baroreflex (Billman, Dickey, Teoh, & Stone, 1981). Each of these would explain the findings of investigators who have reported a reduced arterial and aortic baroreflex in high-fit individuals. Nevertheless, there still exists some controversy in the literature regarding the influence of fitness on BRS. To gain a better understanding of this relationship, it may be more appropriate to examine the results of longitudinal studies that have investigated the effects of exercise training on BRS, as will be done in the following chapter.

Studies assessing muscle sympathetic nerve activity. There have been only been a few studies that have examined the relationship between fitness and MSNA. To make matters more difficult, the results of these studies still remain equivocal. Svedenhag, Wallin, Sundlof, and Henriksson (1984) investigated this relationship by comparing a group (*n*=8) of trained cyclists (age=22±2 yr; VO_{2max}=63.5±1.2 ml•kg^{-1}•min^{-1}) to a group (*n*=8) of age-matched control subjects (age=23±1 yr; VO_{2max}=40.1±1.5 ml•kg^{-1}•min^{-1}). The cyclists and controls exhibited similar levels of MSNA reported as either bursts/100 heart beats (34.8±7 vs. 34.2±7, respectively) or bursts/minute (20.3±4 vs. 22.4±4, respectively), prompting Svedenhag et al. to conclude that MSNA is unrelated to physical fitness. Seals (1991) reported similar findings by comparing a group of endurance athletes (*n*=12; age=25±1 yr; VO_{2max}= 60-75 ml•kg^{-1}•min^{-1}) to a group of untrained individuals (*n*=12; age=27±1 yr). There were no differences in resting MSNA expressed as either bursts/min (athletes: 24±3; controls: 24±2) or bursts/100 heart beats (athletes: 36±3; controls: 44±4). Additionally, there were no group differences in MSNA, expressed as the percent increase of total minute activity, in response to graded LBNP at pressures of –5 (113±8 vs. 132±6), -10 (136±11 vs. 163±8), -15 (174±12 vs. 210±19), and –20 mmHg (209±20 vs. 262±30) between athletes and controls, respectively. Seals also failed to find any differences between groups in the percent increase of total minute activity in response to either isometric handgrip exercise at 30% maximal voluntary contraction (MVC) (athletes: 161±15; controls: 204±34) or the cold pressor test (athletes: 300±29; controls: 255±39). Conversely, in an older population, Ng, Callister, Johnson, & Seals (1994) reported opposite findings. These investigators compared the MSNA of 16 masters endurance athletes (age=66±1 yr; estimated VO_{2max}~42±2 ml•kg^{-1}•min^{-1}) to that of a control group of similar age (*n*=15; age=65±1 yr; estimated VO_{2max}~32±1 ml•kg^{-1}•min^{-1}).

The athletes exhibited significantly higher levels of MSNA at rest compared to the controls when expressed as either bursts/minute (43±2 vs. 32±3) or bursts/100 heart beats (75±4 vs. 52±5). Interestingly, there was also a significant group-by-gender interaction for MSNA such that the magnitude of difference between trained and untrained females was greater than that between trained and untrained males. Ng et al. further measured MSNA during the administration of the cold pressor test and reported no group differences in MSNA, expressed as total activity (athletes: 792±143; controls: 592±121), while reporting a trend for the athletes to exhibit a greater percent increase in MSNA during the test (p=0.06). Additionally, these investigators examined the MSNA response during isometric handgrip exercise to fatigue at 40% of their MVC. The athletes exhibited greater MSNA, expressed as total activity during the handgrip exercise compared to the controls (821±183 vs. 797±164), whereas the percent increase in MSNA did not statistically differ between groups (athletes:200%; controls: 150%). In a study that did not, per se, compare subjects of different fitness levels, but is worthy of discussion, Saito, Watanabe, and Mano (1993) evaluated the MSNA of dominant and nondominant arms of 10 subjects (age=20±2 yr) who were active in racket sports. They reported no difference in the percent increase in MSNA between arms measured during either static handgrip exercise at an intensity of 25% MVC (dominant: 46%; nondominant: 46%), or during dynamic handgrip exercise performed at the same intensity at a rate of 1 Hz (dominant: 38%; nondominant: 36%). However, in 5 subjects, MSNA was assessed during 10 minutes of submaximal dynamic handgrip exercise performed at a rate of 1 Hz and an intensity of 0.9 Watts. In these subjects, the MSNA response was significantly attenuated in the dominant arm relative to the nondominant.

In conclusion, it appears that physical fitness plays a minor role in altering levels of MSNA in young adults. Although Ng et al. (1994) reported higher resting MSNA in older athletes, this difference was gender-related with females demonstrating a greater separation among subjects of different fitness levels. Additionally, since MSNA increases concurrently with age (Ng, Callister, Johnson, & Seals, 1993), it is difficult to compare these findings with other studies using younger subjects. Nonetheless, there is a recognizable lack of research examining this relationship and more studies need to be performed before definite conclusions can be made.

Summary. In conclusion, there is some evidence to suggest aerobic fitness is related to autonomic control of the CV system. Studies using both time and spectral indices of HRV have reported an augmented cardiac vagal modulation in high- compared to low-fit subjects. Furthermore, it appears that aerobic fitness is related to the NE response to submaximal exercise at a given absolute workload, as several studies have reported an attenuated response of NE in high- compared to low-fit individuals. However, the influence of fitness on resting plasma NE and the NE response to exercise at the same relative intensity remains controversial. Additionally, studies examining resting E and the E response to exercise have also provided inconclusive results regarding an effect of fitness. Those studies that have used MSNA and CV reactivity to stress also remain equivocal. Lastly, research suggests that aortic BRS is attenuated in high-fit subjects, while the influence of fitness on carotid and cardiopulmonary BRS is still controversial.

Influence of Endurance Exercise Training on Autonomic Regulation of the Cardiovascular System

It has been well established that endurance exercise training induces many cardiovascular (Clausen, 1977; Ekblom, 1968; Saltin & Astrand, 1967) and metabolic adaptations (Holloszy & Booth, 1976). These include an increase in aerobic capacity (VO_{2max}) (Clausen, 1977), decreases in HR and BP at rest and during submaximal work (Clausen, 1977), favorable alterations in lipid profile, improved glucose tolerance, increased insulin sensitivity, a reduction in body fat, and an increase in lean body mass (Holloszy, & Booth, 1976). In healthy young and middle-aged subjects, the training-induced increase in VO_{2max} is primarily a consequence of an increase in maximal CO and, to a lesser extent, an increase in maximal $(a\text{-}v)O_2$ difference. This increase in CO is a result of an elevated SV at maximal exercise, as maximal HR is not significantly altered with training. Spina (1999) suggested that the elevated maximal SV in the trained state is a result of: 1) an enhanced inotropic state; 2) a greater end-diastolic volume, via either acute changes in end-diastolic and stroke volume (Frank-Starling mechanism), or chronic left ventricular volume overload or eccentric hypertrophy; 3) a reduced left ventricular wall stress; or, 4) a combination of these variables. The enhanced $(a\text{-}v)O_2$ difference is mediated by increases in the aerobic capacity and capillary density of skeletal muscle, leading to an increased oxygen extraction of the muscle.

Some of these adaptations to endurance exercise training may be partly accounted for by training-induced changes in autonomic system activity. Therefore, this section of the review will provide a comprehensive review of studies that have assessed measures of autonomic activity before and after an endurance exercise training protocol.

Studies assessing the CV response to laboratory stressors. Studies assessing the effects of endurance exercise training on the CV response to laboratory stressors have yielded mixed conclusions. A summary of results from such studies can be seen in Table 6.1. Several investigators have provided results that support the hypothesis that endurance training attenuates the CV response to stressful stimuli (Blumenthal et al. 1988; Blumental et al. 1990; Bond et al. 1999; Cleroux, Peronnet, & de Champlain, 1985; De Geus, Van Doornen, & Orlebeke, 1993; Holmes & McGilley, 1987; Keller & Seraganian, 1984; Ketelhut, Franz, & Scholze, 1997; Rogers, Probst, Gruber, Berger, & Boone, 1996; Sherwood, Light, & Blumenthal, 1989; Sinyor, Golden, Steinert, & Seraganian, 1986; Stein, & Boutcher, 1992), while others have failed to produce such evidence (De Geus, Van Doornen, De Visser, & Orlebeke, 1990; Roskies et al. 1986; Sinyor, Peronnet, Brisson, & Seraganian, 1988; Sothmann, Hart, & Horn, 1992; Steptoe, Moses, Mathews, & Edwards, 1990). Obviously, the conflicting results of these studies hinders one's ability to draw clear conclusions regarding the effects of exercise training on CV reactivity. However, by examining each study carefully, some conclusions can be made. For example, most studies that have shown a beneficial effect of training on CV reactivity have used subjects with a pre-existing condition. Several studies have used subjects classified as having a type-A personality. In this population, Blumenthal et al. (1988) reported that 12 weeks of walking/jogging at 70% VO_{2max} attenuated the HR, SBP, DBP, and myocardial oxygen demand (MVO_2) response to a mental arithmetic task. In a separate study using the same training protocol, Blumental et al. (1990) demonstrated that endurance training resulted in decreased HR, DBP, and MVO_2 reactivity to the same mental arithmetic task in type A men. Sherwood et al. (1989) further demonstrated that 12 weeks of aerobic training reduced DBP reactivity to a 5-minute

Table A.6

Longitudinal Studies Assessing the Effects of Endurance Training on Cardiovascular Responses to Laboratory Stressors.

Author/Date	Training protocol (mode; time period; frequency; duration; intensity)	Stressor	Results
Blumenthal et al. (1990)	Walk/jog; 12-wk; 3x/wk; 30 min; 70% $HR_{reserve}$	Mental arithmetic	HR, DBP, & RPP reactivity ↓ post-training
Blumenthal et al. (1988)	Walk/jog; 12-wk; 3x/wk; 30 min; 70% $HR_{reserve}$	Mental arithmetic	HR, SBP, DBP, & RPP reactivity ↓ post-training
Bond et al. (1999)	Jogging; 6-wk; 3x/wk; 35 min; 60-70% VO_{2peak}	Cold pressor test	SBP & MAP reactivity ↓ post-training
Cleroux et al. (1985)	Jogging; 20-wk; 3x/wk; 45 min; 60% VO_{2max}	Video game	MAP reactivity ↓ post-training
de Geus et al. (1990)	Jogging; 7-wk; 4x/wk; 20-60 min; 70% VO_{2peak}	Reaction time task	No change in HR, BP, or TPR reactivity

HR = heart rate
SBP = systolic blood pressure
DBP = diastolic blood pressure
MAP = mean arterial pressure
CO = cardiac output
TPR = total peripheral resistance
E = epinephrine
NE = norepinephrine
CWCT = color word conflict test
RPP = rate pressure product
↓ = decrease
↑ = increase

Table con'd.

Table A.6

Author/Date	Training protocol (mode; time period; frequency; duration; intensity)	Stressor	Results
de Geus et al. (1993)	Jogging; 8-mo; 4x/wk; 20-60 min; 70% VO_{2peak}	Reaction time task	TPR reactivity ↓ and CO reactivity ↑ post-training
Holmes et al. (1987)	Aerobic dance; 13-wk; 2x/wk; 50 min; 70% $HR_{reserve}$	Mental arithmetic	HR reactivity ↓ in low-fit subjects post training
Keller & Seraganian (1984)	calisthenics/running; 10-wk; 4x/wk; 30 min; unspecified intensity	Stroop CWCT	Faster recovery of HR post training
Ketelhut et al. (1997)	Running; 18-mo; 2x/week; 1-hr; 70%HRmax	Cold pressor test	DBP reactivity ↓ post training
Rogers et al. (1996)	Walk/jog; 8-wk; 3x/wk; 45 min; low group: 40-50% VO_{2max}, moderate group: 70-80% VO_{2max}	Stroop CWCT	Low: ↓ MAP, SBP, & DBP reactivity; Mod: ↓ DBP reactivity
Roskies et al. (1986)	Jogging; 30 sessions; 20-25 min; 50-85% $HR_{reserve}$	Mental arithmetic	No change in HR, SBP, or DBP reactivity
Sherwood et al. (1989)	Walk/jog; 12-wk; 3x/wk; 30 min; 60-75% HR_{max}.	Reaction time task	DBP reactivity ↓ post-training

Table con'd.

Table A.6

Author/Date	Training protocol (mode; time period; frequency; duration; intensity)	Stressor	Results
Sinyor et al. (1986)	Jogging; 10-wk; 3x/wk; 60 min; 60% VO_{2max}	Mental arithmetic Tone avoidance	Faster HR recovery post training
Sinyor et al. (1988)	Jogging; 10-wk; 3x/wk; 60 min; 60% VO_{2max}	Mental arithmetic Stroop CWCT	No change in HR, E, or NE reactivity post training
Sothmann et al. (1992)	Jogging; 16-wk; 3x/wk; 25-30 min; 70-75% VO_{2max}	Stroop CWCT	No change in HR, E, or NE reactivity post training
Stein et al. (1992)	Walk/jog; 8-wk; 3x/week; 20-30 min; 60% $HR_{reserve}$	Stroop CWCT	HR reactivity ↓ post training
Steptoe et al. (1990)	Walk/jog; 10-wk; 4x/wk; 20-30 min; high group: 70-75% HR_{max}, moderate group: 60-65% HR_{max}.	Problem solving	No change in HR or BP reactivity in either group

competition task in Type A men who were classified as borderline hypertensive. Additionally, De Geus et al. (1993) reported that 8 months of training reduced TPR reactivity in type-A males. Other studies showing improvement following training have used hypertensive subjects. For example, Cleroux et al. (1985) showed an improved MAP reactivity to video game stress in labile hypertensives after training. Furthermore, Ketelhut et al. (1997) and Rogers et al. (1996) both reported a training-induced improvement of BP reactivity in this population. Thus, these studies possibly suggest that exercise endurance training improves CV reactivity in subjects with a pre-existing condition. Holmes and McGilley (1987) also provided data suggesting that training improves HR reactivity to the recall of digits backwards test of the Wechsler Adult Intelligence Scale in low-fit, but not high-fit, subjects, identified by their performance on a 12-minute walk/run test. The data of Holmes and McGilley further support the hypothesis that a pre-existing condition (low fitness level) may account, in part, for training-induced improvements in CV reactivity.

Another factor that necessitates consideration is the volume of training. With the exception of one study (Sothmann et al., 1992), all studies that have employed greater than 12 weeks of training have shown improvement in CV reactivity, suggesting that there may be a training threshold for CV adaptation. Although both Keller et al. (1984) and Sinyor et al. (1986) reported improvements in the HR recovery from a stressor following training periods of 9 and 10 weeks respectively, it should be noted that neither were able to show any improvements in the magnitude of the CV response to stress. Additionally, Stein and Boutcher (1992) showed improvements in HR reactivity after training, but failed to demonstrate any beneficial effects on BP reactivity. Lastly, Bond et al. (1999) reported that 6 weeks of training yielded improvements in BP reactivity, but failed to show any effect on HR

or TPR reactivity. Furthermore, it is difficult to compare this group's results to others because this was the only study to examine training-induced alterations in CV reactivity in African-American women. In conclusion, research is inconclusive as to the influence of exercise endurance training on CV reactivity. When examining this issue, one must carefully consider the subject population and the specifics of the training protocol utilized. Lastly, it is possible that other methodologies may be more sensitive in detecting autonomic changes induced by endurance training.

Studies assessing plasma catecholamines. As previously stated, SNS activity can be assessed by monitoring plasma catecholamine kinetics at rest and during physiological perturbations. Thus, several investigations have used this technique to gain a better understanding of autonomic changes induced by exercise endurance training. Studies assessing the effects of exercise training on resting catecholamine levels have provided mixed results (Table 6.2). Some studies indicate that resting catecholamine concentration is unaffected by endurance training (Cousineau et al. 1977; Hartley et al. 1972a; Hartley et al. 1972b; Peronnet et al. 1981; Greiwe, Hickner, Shah, Cryer, & Holloszy, 1999; Brundin & Cernigliaro, 1975; Cleroux, Peronnet, & De Champlain, 1984; Cleroux, Peronnet, &De Champlain, 1985; Ehsani et al. 1984; Hagberg et al. 1984; LeBlanc, Nadeau, Richard, & Tremblay, 1982; Lehmann, Dickhuth, Schmid, Porzig, & Keul, 1984; Schwartz, Jaeger, Veith, & Lakshminarayan, 1990; Svedenhag, Martinsson, Ekblom, & Hjemdahl, 1986; Winder et al. 1978), while others have reported a reduction (Bloom, Johnson, Park, Rennie, & Sulaiman, 1972; Cooksey, Reilly, Brown, Bomze, & Cryer, 1978; Duncan et al. 1985; Jennings et al. 1986; Jost, Weiss, & Weicker, 1989; Jost, Weiss, & Weicker, 1990; Kiyonaga, Arakawa, Tanaka, & Shindo, 1985; McCrimmon, Cunningham, Rechnitzer, & Griffiths,

Table A.7

Longitudinal Studies Assessing the Influence of Endurance Exercise Training on Resting Catecholamine Levels.

Author/Date	Training Protocol (mode; time period; frequency; duration; intensity)	Findings
Brundin & Cernigliaro (1975)	cycling; 2-mo; protocol unspecified	↔ in NE or E
Cleroux et al. (1985)	jogging; 20-wk; 3x/wk; 45 min; 60% VO_{2max}	↔ in NE or E
Cleroux et al. (1987)	cycling or running 20-wk; 3x/wk; 20-45 min; 60% $HR_{reserve}$	cycle: ↓ E ↔NE; run: ↔NE or E
Cooksey et al. (1978)	walk/jog; 12-wk; 3x/wk; 50 min; 60-70% HR_{max}	↔ in E; ↓ in NE
Cousineau et al. (1977)	cycling/volleyball; 6-mo; 2-3x/wk; 50 min; unspecified intensity	↔ in E or NE
Duncan et al. (1985)	walk/jog; 16-wk; 3x/wk; 60 min; 70-80% HR_{max}	↔ in E; ↓ in NE
Ehsani et al. (1984)	walk/jog/cycle; 12-mo; 3-5x/wk; 30-60 min; 50-90% VO_{2max}	↔ in NE or E
Greiwe et al. (1999)	cycling/running; 10-wk; 6x/wk; 30-40 min; cycle: 90-100%VO_{2max}, run: highest tolerable pace	↔ in NE or E

NE = norepinephrine
E = epinephrine
SP = spillover
↓ = decrease
VO_2 = oxygen consumption
HR = heart rate
↔ = no change

table con'd.

Table A.7

Author/Date	Training Protocol (mode; time period; frequency; duration; intensity)	Findings
Hagberg et al. (1984)	walk/jog/cycle; 8-mo; 3-5x/wk; 30-45 min; 60-65% VO_{2max}	↔ in NE or E
Hartley et al. (1972a)	running/basketball/volleyball; 7-wk; 3x/wk; 3-hr; HR of 145-180 bpm	↔ in NE or E
Jennings et al. (1986)	cycling; 4-wk; 3x/wk or 7x/wk; 60-70% of maximal work capacity	↓ NE SP in both
Jost et al. (1990)	run/swim; 6-wk; 6-7x/wk; run: 95±6 km/wk, swim: 30.6±2 km/wk	run: ↓ NE swim: ↓ E
Kiyonaga et al. (1985)	cyling; 20-wk; 3x/wk; 60 min; workload was set at 1st breaking point of lacate	↓ E & NE
McCrimmon et al. (1976)	calisthenics/jog; 27-wk; frequency and duration unspecified; 65-70% VO_{2max}	↓ NE
Peronnet et al. (1981)	cycling; 20-wk; 3x/wk; 30-min; 80% HR_{max}	↔ in NE
Schwartz et al. (1990)	walk/jog; 3-mo; 3x/wk; 40 min; 70-85% $HR_{reserve}$	↔ in NE or E
Svedenhag et al. (1986)	run/cycle; 4-mo; 4x/wk; duration & intensity unspecified	↔ in NE or E
Urata et al. (1987)	cycling; 10-wk; 3x/wk; 60 min; HR ~101 bpm	↔ in E; ↓ in NE
Winder et al. (1978)	cycling/run; 7-wk; 6x/wk; 30-40 min; cycle: 90-100% VO_{2max}, run: highest tolerable pace	↔ in NE or E

1976; Urata, Tanabe, & Kiyonaga, 1987). The discrepancies in the findings of these studies possibly suggest that the catecholamine response to stressful stimuli (i.e. mental tasks, exercise) may be a better indicator of SNS drive, as levels may be too low during rest to accurately detect any changes due to training. Accordingly, investigators have assessed the influence of endurance training on the catecholamine response to physiological perturbations. As in the previous chapter, time constraints limit this review to those studies that have used exercise and psychological stimuli as perturbations to elicit a catecholamine response.

Studies that have utilized submaximal exercise to elicit a catecholamine response have used two basic techniques: 1) those that monitor catecholamine kinetics during the same absolute workload pre- and post-training; and, 2) those that monitor catecholamine kinetics during the same relative workload pre- and post-training. Researchers using the former have provided evidence for a reduced catecholamine response to submaximal exercise following endurance training in healthy individuals (Greiwe et al. 1999; Hartley et al. 1972b; Peronnet et al. 1981; Winder et al. 1978; Winder et al. 1979). Hartley et al. (1972b) reported that the NE response to 40 minutes of cycling at a specific workload (~75% of initial VO_{2max}) was significantly attenuated following training (2.9±0.3 vs. 4.2±0.5 ug•l^{-1}) in a group of young subjects (*n*=7; age=20-24 yr). They further reported a reduced NE response to near-maximal exercise following training, although E levels were not different at any workload following training. In this investigation, training elicited an increase in VO_{2max} from 2.95 to 3.36 l•min^{-1}, so the actual %VO_{2max} at which the subjects were working during the 40 minutes of exercise was lower after training (61.3 vs. 72.6 %). In an attempt to determine the time course of these changes, Winder et al. (1978) assessed the effects of a 7-week training protocol on the catecholamine response to cycle ergometry (95% of initial VO_{2max}) in a group

of healthy males (*n*=6; age=30±1 yr), evaluating the subjects at weekly intervals. Both the NE and E response to exercise at the same absolute workload were significantly reduced after only 1 week of training. Both continued to decrease with training until a plateau was reached after the 3rd week, after which there were no further decreases despite intensity increases in the training protocol. In a subsequent study using a similar training protocol, Winder et al. (1979) further reported that 9 weeks of training resulted in a decreased NE and E response to a given workload (850±74 kpm•min^{-1}) of cycle ergometry exercise in what appears to be the same group of subjects. Peronnet et al. reported similar findings in a group of healthy males (*n*=10; age=37±2 yr) following 20 weeks of training that elicited a significant increase in VO_{2max} (33±2 vs. 42±1 ml•kg^{-1}•min^{-1}). They noted a reduced plasma NE response (687±64 vs. 1371±286 pg•ml^{-1}) to cycling at a set submaximal workload (735±51 kg•m•min^{-1}) post-compared to pre-training. Most recently, Greiwe et al. (1999) reported that 10 weeks of training, sufficient to increase VO_{2max} from 39.2±8 to 46.9±8 ml•kg^{-1}•min^{-1}, led to reductions in NE (956±170 vs. 1264±160 pg•ml^{-1}) and E (76±9 vs. 146±26 pg•ml^{-1}) at an identical workload to that before training in previously untrained subjects (*n*=9; age=28±8 yr). These findings have also been extended to both the hypertensive population (Hagberg et al. 1984; Urata et al. 1987) and patients with heart disease (Cooksey et al. 1978; Cousineau et al 1977; Ehsani et al. 1984).

Alternatively, the effect of endurance training on the catecholamine response to exercise at a percentage of a subject's VO_{2max} is still unclear. Results of studies addressing this issue have been inconsistent, with some reporting no change (Brundin & Cernigliaro, 1975; Peronnet et al. 1981;Winder et al. 1979), others reporting a decrease (Hartley et al. 1972a), and others reporting an increase (Cleroux et al. 1987; Cooksey et al. 1978; Ehsani et

al. 1984; Greiwe et al. 1999; Hagberg et al. 1984; Winder et al. 1978). Greiwe et al. recently reported a significantly increased NE response to exercise intensities of 65, 70, 75, 80, and 85% VO_{2max} following 10 weeks of cycle ergometer training and running. Although, the E response was not significantly different at any exercise intensity following training, there was a trend for the post-training E response to be greater at intensities of 80 and 85% VO_{2max}. They hypothesized that the increased NE response was mediated by the use of a larger skeletal muscle mass resulting in a greater stimulation of afferent nerves. Cleroux et al. reported that 20 weeks of cycling training (n=7; age=37±4 yr) did not influence the response to NE or E to cycling at 60% VO_{2max}. However, another group of subjects (n=5; age=32±4 yr) that used running as the mode of training exhibited an elevated E response to cycling at 60% VO_{2max}, and nearly significantly elevated NE responses (~+1000 $pg \bullet ml^{-1}$). Interestingly, the cycle ergometer training and running elicited improvements in VO_{2max} of 13 and 21%, respectively. Thus, the differences in findings between groups may be a result of different training effects of the 2 different exercise modalities. Winder et al. (1978) demonstrated a significant increase in both the NE and E response to exercise at similar relative workloads following their training protocol. They reported a NE concentration of 4.04±0.7 $ng \bullet ml^{-1}$ at approximately 100% VO_{2max} after training compared to 2.95±0.3 $ng \bullet ml^{-1}$ at 95% VO_{2max} prior to training. Similar results were reported for plasma E (1.24±0.2 vs. 0.53±0.1 $ng \bullet ml^{-1}$). However, the use of slightly different workloads pre- and post-training (95 vs. 100% VO_{2max}) makes it difficult to draw clear-cut conclusions from this investigation. Hagberg et al. further reported an elevated NE response to exercise at 60% VO_{2max} in young essential hypertensives (n=12; age=16±1 yr) following 8 months of training that was sufficient to increase VO_{2max} from 41.0±3 to 46.5±3 $ml \bullet kg^{-1} \bullet min^{-1}$. In patients with coronary artery disease (n=21;

age=50±8 yr), Ehsani et al. reported that 12 months of training that increased VO2max by 42% resulted in an increase in the NE response to maximal exercise (3642±1500 vs. 2049±704 pg•ml^{-1}), although no changes in the E response were noted. In a similar population (*n*=10; age=40-55 yr), Cooksey et al. also reported an increased NE (3003±101 vs 2120±77 pg•ml^{-1}) and E (323±23 vs. 155±15 pg•ml^{-1}) response to maximal exercise following exercise training that significantly improved treadmill time to exhaustion (374±28 to 567±33 seconds).

Alternatively, Winder et al. (1979) reported no change in plasma NE or E at the same relative workload following 9 weeks of endurance training. However, this group used 62% VO_{2max} as the relative workload which may have been too low an intensity to detect any training-induced changes in the NE response. Although Peronnet et al. did not report a significant change in the NE response to exercise at an intensity that elicited a HR of ~157 bpm, it should be noted that NE was higher following training (1371±286 vs. 1729±371 pg/ml). Additionally, the intensity of HR~157 bpm may not have been sufficient to detect training-induced changes. Similarly, Brundin & Cernigliaro failed to find any differences in the urinary NE and E response to exercise following 2 months of cycle ergometer training. However, there are several methodological concerns that should be addressed regarding their investigation. In this study, urinary catecholamine levels were measured after the subjects cycled at a moderate intensity (HR ~ 140 beats•min^{-1}) for 30 minutes, followed by a near maximal effort for 7 minutes. Thus, the catecholamine concentrations that they measured actually reflected the response to maximal exercise. Furthermore, their failure to report the workload at which the subjects were exercising at near-maximal effort prevents one from drawing definite conclusions. Lastly, the training protocol utilized in this study was poorly

described with regards to frequency, duration, and intensity. Nevertheless, if one examines Brundin and Cernigliaro's data carefully, there was a slight, although not statistically significant, increase in the NE response to exercise following training (32±3.2 vs. 27 ±1.5 ng•mg excreted creatinine^{-1}), which is consistent with other investigations (Cleroux et al.; Cooksey et al.; Ehsani et al.; Greiwe et al.; Hagberg et al.; Winder et al. 1978). Although, Hartley et al.'s (1972a) finding of a reduced NE response at moderate and heavy exercise following training also remains controversial, it should be pointed out that the pre-training workloads (75 and 98% of VO_{2max}), were slightly higher than the post-training workloads (71 and 93% VO_{2max}). In conclusion, research suggests that endurance exercise training that elicits improvements in VO_{2max} results in an attenuation of the catecholamine response to exercise at the same absolute workload. Furthermore, although there is ample evidence that the catecholamine response to exercise at the same relative workload (i.e. percentage of VO_{2max}) is elevated following training, there still exists some controversial data and more research must be done before definite conclusions can be made.

Studies using the catecholamine response to psychological stimuli in humans have had little success in showing a training effect. For example, Cleroux et al. (1984) demonstrated that 20 weeks of jogging (3x/wk; 45 min/day; 60% VO_{2max}) resulted in no change in the E or NE response to a video game task. Similarly, Sinyor, Peronnet, Brisson, & Seraganian (1988) found no changes in catecholamine reactivity to mental arithmetic tasks or to the Stroop CWCT following 10 weeks of jogging (3x/wk; 60 min/day; 60% VO_{2max}). Furthermore, Blumenthal et al. (1990) reported no changes in catecholamine reactivity to mental arithmetic following 12 weeks of training (walk/jog; 3x/wk; 30 min/day; 70% $HR_{reserve}$). There is, however, some evidence to suggest that catecholamine reactivity is suppressed following

endurance training in rats (Cox, 1991). Cox reported that 12 weeks of swimming (2-hour/day) resulted in an attenuation of the NE response to 30 minutes of cutaneous tail shock. However, one must use caution when comparing animal studies with those done in humans because of the type of stress used (mental vs. shock) and the differences in training modalities (training studies in rats are consistently more vigorous than those in humans).

Studies assessing the variability of heart rate and blood pressure. Several recent studies have used HRV to make inferences about the influence of endurance exercise training on autonomic control of the heart. An outline of these studies can be seen in Table 6.3. In healthy individuals, several investigators have reported improvements of HRV indices with training (Al-Ani, Munir, White, Townend, & Coote, 1996; DeMeersman, 1992; Levy et al. 1998; Schuit et al. 1999; Seals & Chase, 1989; Stein, Ehsani, Domitrovich, Kleiger, & Rottman, 1999). In nine track athletes, De Meersman reported that 8-weeks of intense running significantly increased both VO_{2max} (7.2%) and SDNN (23.1%). In 11 young adult males, Al-Ani et al. reported that 6 weeks of cycle ergometer exercise was sufficient to reduce resting HR by 12 beats/min and increase VO_{2max} (15%). Furthermore, training resulted in increases in RSA, and LF and HF spectral power in 9 subjects. However, in two others, opposite findings were reported. It was concluded from this study that the reduction in resting HR was a result of increased cardiac vagal tone. Seals and Chase examined the effects of a 30-week training protocol on HRV in a group of middle-aged to older males (n=11) compared to a control group (n=8) of a similar age range. Training resulted in a 25% increase in VO_{2max} and a significant reduction in resting HR, while these variables were unchanged in the control group. Additionally, exercise training resulted in a significant increase in SDNN and a nonsignificant increase in RSA. Similar to Al-Ani, these researchers concluded that a

Table A.8

Studies Examining the Influence of Endurance Exercise Training on Heart Rate Variability

Author/Date	Population (Age)	Training Protocol (mode; time period; frequency; duration; intensity)	Findings
Al-Ani et al. (1996)	Healthy (20±1 yr)	cycling; 6-wk; 7x/wk; 25-min; 85% HR_{max}	↑RSA, ↑HF, ↑LF
Bonaduce et al. (1998)	Cyclists (21±4 yr)	cycling; 5-mo; 5x/wk; 4-hr; unspecified	↔SDNN, ↔rMSSD, ↔pNN50, ↔LF, ↔HF, ↔LF/HF
Boutcher & Stein (1995)	Healthy (46±1 yr)	walk/jog; 8-wk; 3x/wk; 20-30 min; 60% $HR_{reserve}$	↔RSA, ↔HF, ↔LF
Coats et al. (1992)	Heart Failure (62±2 yr)	cycling; 8-wk; 5x/wk; 20 min; 60-80% HR_{max}	↑SDNN, ↑HFnu, ↓LFnu
Davy et al. (1997)	Post-menopausal hypertensive (55±1 yr)	walk; 12-wk; 3-4x/wk; 30-45 min; 60-75% HR_{max}	↔SDNN, ↔TP, ↔LF, ↔HF
Deligiannis et al. (1999)	Renal Disease (48±12 yr)	stepping/swimming/games; 6-mo; 3-4x/wk; 50-min; 60-70% HR_{max}	↑SDNN, ↑ triangular index

RSA = respiratory sinus arrhythmia
LF = low-frequency power
TP = total power
SDNN, SDANN, rMSSD, pNN50 = see text
HF = high-frequency power
nu = normalized units

Table Con'd.

Table A.8

Author/Date	Population (Age)	Training Protocol (mode; time period; frequency; duration; intensity)	Findings
De Meersman (1992)	Healthy (18-22 yr)	running; 8-wk; 7x/wk; 90-120 min; 75-90% HR_{max}	↑SDNN
Fujimoto et al. (1999)	Post-MI (59±11 yr)	cycling; 2-wk; 2x/day; 10-min; 80% anaerobic threshold	↑SDNN, ↑SDANN, ↑HF, ↓LF/HF
Gutin et al. (1997)	Obese children (9.6±0.2 yr)	Unspecified; 4-mo; 5x/wk; 40-min; HR~153 bpm	↑rMSSD, ↓LFnu, ↓LF/HF
Howorka et al. (1997)	Diabetic (50±9 yr)	cycling; 12-wk; 2x/wk; 30-min; 65%$HR_{reserve}$	↑LF, ↑HF, ↑TP (except for those with severe autonomic neuropathy
Kiilavuori et al. (1995)	Heart Failure (52±8 yr)	cycling; 3-mo; 3x/wk; 30 min; 50-60% VO_{2peak}	↑HF, ↓LF/HF
La Rovere et al. (1992)	Post-MI (47±6 yr)	cycling; 4-wk; unspecified frequency & duration; 75-95% anaerobic threshold	↑ LF/HF during head-up tilt
Leitch et al. (1997)	Post-MI (56±1 yr)	cycling; 6-wk; 3-4x/wk; 30-60 min; 70% HR_{max}	↑SDNN, ↑SDANN, ↑TP, ↑LF, ↑HF
Levy et al. (1998)	Healthy (24-32 & 60-92 yr)	walk/jog/cycling; 6-mo; 4-5x/wk; 45-min; 50-85% $HR_{reserve}$	↑SDNN in both age groups

Table Con'd.

Table A.8

Author/Date	Population (Age)	Training Protocol (mode; time period; frequency; duration; intensity)	Findings
Maciel et al. (1985)	Healthy (29±1 yr)	cycling; 10-wk; 5x/wk; 4 6-min periods at 60, 70, 80. 90% HR_{max}	↔ RSA
Malfatto et al. (1996)	Post-MI (52±7 yr)	cycling; 8-wk; 5x/wk; 60-min; 80%HR_{max}	↑SDNN, ↑rMSSD, ↑pNN50, ↓LF/HF
Oya et al. (1999)	Post-MI (59±6 yr)	cycling; 2-wk; 14x/wk; 30 min; anaerobic threshold	↑HF
Radaelli et al. (1996)	Heart Failure (55+3 yr)	cycling; 5-wk; 5x/wk; 30 min; 60-70% VO_{2max}	↑HFnu; ↓LF/HF
Schuit et al. (1999)	Healthy (67±5 yr)	walk/jog/games; 6-mo; 3x/wk; 45 min; 60-80% HR_{max}	↑SDNN, ↑very-LF, ↑LF
Seals & Chase (1989)	Healthy (53±2 yr)	walk/jog; 30-wk; 3-4x/wk; 45-min; 80%$HR_{reserve}$	↑SDNN, ↔ RSA
Stahle et al. (1999)	Post-MI (71±4 yr)	cycling (intervals); 3-mo; 3x/wk; 50-min; three 4-min peaks at >85% HR_{max}	↑SDNN, ↑SDANN
Stein et al. (1999)	Healthy (66±4 yr)	walk/jog/cycling/rowing; 9-mo; 5x/wk; 45-60 min; 60-85% VO_{2max}	↑SDNN, ↑SDANN, ↑TP, ↔rMSSD, ↔pNN50, ↔LF, ↔HF

training-induced increase in cardiac vagal tone was responsible for the post-training reduction in resting HR. Levy et al. examined the effect of 6 months of endurance training on a group of young adults (24-32 yr; *n*=11) and a group of older adults (60-82 yr; *n*=13). In this study, exercise training led to increases in VO_{2max} of 21% and 17%, and reductions in resting HR of ~9 and ~5 beats/min in the older and younger groups, respectively. Furthermore, SDNN was increased by 68% and 17%, respectively, in the older and younger subjects. With this data, it was concluded that there was a training induced increase in cardiac parasympathetic drive, as plasma catecholamine levels were unchanged with training. Stein et al. examined the effects of a 9-month training protocol on HRV in a group of older men (*n*=7) and women (*n*=9). Training resulted in an increased VO_{2max} of 30.5% and a slight nonsignificant reduction of resting HR (*p*=0.08). Additionally, training resulted in significantly increased SDNN (13%), SDANN (11%), and TP (3%), although pNN50, rMSSD, LF, and HF were unchanged. Furthermore, a comparison (non-training) group was evaluated in this study and demonstrated no alterations in HRV indices over the course of the study. Another study examining the effects of endurance training on HRV indices in older men (*n*=14) and women (*n*=13) was performed by Shuit et al. In this investigation, 6-months of training resulted in a significant increase in VO_{2max} in comparison to a control group of a similar age. However, there was no difference in resting HR between pre- and post-training. With regards to HRV, training resulted in higher SDNN, LF, and very-LF power, although pNN50 and HF were unchanged with training.

In contrast, a few studies in healthy individuals have failed to demonstrate an effect of endurance exercise training on HRV (Bonaduce et al. 1998; Boutcher & Stein, 1995; Maciel et al. 1985). Maciel et al. examined the effect of 10-weeks of endurance training on the RSA

in a group of previously sedentary males (*n*=7). Training led to a significant increase in VO_{2max} (16%) and a ~11 beat/min decrease in resting HR. However, this group failed to find a difference in RSA following training. Interestingly, these investigators also used the vagal blocker atropine to further quantify any training-induced changes in sympathovagal balance and reported no pre-post differences in the HR response to atropine infusion. Therefore, it is possible that the training protocol was insufficient to elicit alterations in autonomic balance. Bonaduce et al. studied the effects of 5-months of intensive cycle training on a group of high level cyclists (*n*=15). There was a significant training-induced increase in VO_{2max} (8%), along with a significant reduction in resting HR of ~5 beats/min following training. However, there was no evidence of any training-induced alterations in HRV indices. It should be noted that a possible confounding factor in this study was the initial fitness levels of the subjects (VO_{2max} = 62±4 ml•kg^{-1}•min^{-1}). Therefore, the high initial fitness level of these subjects possibly masked any training-related alterations in HRV parameters. Boutcher and Stein also were unable to detect any training-related changes in RSA, LF, or HF in a group of sedentary middle aged men (*n*=19). Although the 8-week training protocol used was sufficient to significantly increase VO_{2max}, and reduce resting HR, these changes were minimal (11% and 4%, respectfully). Therefore, it may be possible that the training protocol was not intense enough to alter HRV indices.

The majority of intervention studies investigating the effect of endurance exercise training on HRV have been performed in clinical populations (Davy, Willis, & Seals, 1997; Deligiannis, Kouidi, & Tourkantonis, 1999; Fujimoto et al. 1999; Gutin, Owens, Slavens, Riggs, & Treiber, 1997; Howorka et al. 1997; Kiilavuori, Toivonen, Naveri, & Leinonen, 1995; La Rovere, Mortara, Sandrone, & Lombardi, 1992; Leitch et al. 1997; Malfatto et al.

1996; Oya, Itoh, Kato, Tanabe, & Murayama, 1999; Radaelli et al. 1996; Stahle, Nordlander, & Bergfeldt, 1999). Of these, many have examined the effects of exercise training on HRV indices in patients who have had a recent myocardial infarction (MI), as studies have indicated that this population exhibits significantly reduced cardiac variability (Task Force of the European Society of Cardiology & the North American Society of Pacing and Electrophysiology, 1996). For the most part, the literature suggests that exercise training has a positive effect of HRV indices in this population. For example, Malfatto et al. reported that 8-weeks of exercise training favorably improved SDNN, pNN50, rMSSD, and the balance of LF to HF power in a group of post-MI patients (*n*=22), while a group of similar health status that did not train exhibited no changes. Interestingly, after a one-year follow-up of these same patients, the training group still displayed enhanced HRV compared to the others. Similarly, Stahle et al. found that 4 months of endurance exercise training increased SDNN and SDANN in patients (*n*=29) following an acute myocardial infarction, with no changes in a group of control subjects (*n*=36) of a similar age and health status. Furthermore, they also noted a training-related increase in total and HF power in the training group. In another study, Oya et al. reported that 2-weeks of cycling (twice daily) was sufficient to improve HF power in a group of post-MI subjects (*n*=16), with no changes reported in a control group of similar health status (*n*=12). However after 3 months of follow-up, there were no longer significant differences between groups indicating the importance of remaining physically active. Fujimoto et al. also reported that a group of subjects with a recent MI who underwent a 4-week training protocol (*n*=20) exhibited higher HF and lower LF/HF compared to a control group of similar health status (*n*=20). Each of the aforementioned studies suggests a beneficial effect of exercise training on HRV indices in subjects with a recent MI, therefore

potentially demonstrating a protective role of exercise training in this population. However, Leitch et al. failed to demonstrate a significant difference between a group of post-MI patients who underwent 6-weeks of exercise training (*n*=26) and a group who did not (*n*=23). However, in this study both groups increased their HRV indices (SDNN, SDANN, TP, LF, & HF) over the 6-week period. It should also be noted that the control group participated in a home-based walking program and therefore, actually did train. Thus, this study demonstrates the importance of engaging in some type of activity following MI. Lastly, La Rovere et al. reported that 4 weeks of exercise training resulted in an increased LF/HF during head-up tilt in a group of post-MI patients (*n*=11), while a control group of similar health status (*n*=11) did not show any such changes. The authors concluded that this enhanced vagal withdrawal is possibly a result of an improved BRS following training.

Other investigators have examined the effects of exercise training on HRV in other clinical populations. In patients with chronic heart failure (*n*=17), Coats et al. (1992) reported that 8-weeks of training improved vagal modulation of the heart, expressed by increases in SDNN and HFnu and decreases in LFnu. Also in a heart failure population (New York Heart Association Class II and III), Kiilavuori et al. (1995) reported that 3 months of training led to improvements in HF and decreased LF/HF (*n*=8) during the day, while a control group of similar health status (*n*=12) exhibited no alterations in HF and an increase in LF/HF. However, there were no group differences in HRV at night. With these data, the investigators suggested that lack of involvement in a structured exercise program may actually result in an unhealthy sympathovagal balance. Additionally in this population (*n*=6), Radaelli et al. (1996) reported increased HFnu and reduced LF/HF following 5 weeks of home based cycle ergometer training. In diabetic patients with various degrees of autonomic neuropathy,

Howorka et al. (1997) reported that 12 weeks of training increased TP, LF and HF in diabetics without (*n*=8), and those with early signs of neuropathy (*n*=8). However, training had no effect on indices of HRV in those diabetics with severe neuropathies (*n*=6). Thus, it was concluded from this study that exercise training has a beneficial effect on autonomic balance in diabetics with early or no signs of autonomic neuropathy. In hemodialysis patients with end-stage renal disease, Deligiannis et al. (1999) demonstrated a positive effect of exercise training on HRV indices. These investigators reported that 6 months of training resulted in increased SDNN and the triangular index (total number of RR intervals divided by the height of the histogram of all RR intervals) in a group of patients (*n*=30) compared to a control group of similar health status (*n*=30). In post-menopausal hypertensive women (*n*=8), Davy et al. (1997) failed to report any significant changes in HRV following 12 weeks of training. The authors of this study then suggested that their lack of significant findings in HRV indices following training may have been due to an insufficient training stimulus. Lastly, in a group of obese children (*n*=17) Gutin et al. (1997) reported that 4 months of training resulted in significant increases in rMSSD and decreases in LF normalized units and LF/HF compared to a control group of similar subjects (*n*=18). With these data, the investigators concluded that exercise training enhances vagal modulation of the heart in this population. In conclusion, the majority of studies that have examined the influence of physical training on HRV suggest that training has a beneficial effect on autonomic modulation of the heart. Furthermore, it appears that changes in HRV following training are more pronounced in populations in which HRV is initially depressed.

Studies assessing baroreflex sensitivity. Longitudinal studies assessing the influence of exercise endurance training on BRS have produced inconclusive results. Some researchers

have reported findings to suggest an attenuation of BRS following training (Bedford & Tipton, 1987; Negrao et al. 1993; Paynter, Tipton, & Tcheng, 1977; Raven & Stevens, 1990; Stevens, Foresman, Shi, Stern, & Raven, 1992; Tipton, Matthes, and Bedford, 1982), while others have reported either increases (Convertino et al. 1990; Grassi, Seravalle, Calhoun, & Mancia, 1994; Guo, Yi, Batchvarov, Gallagher, & Malik, 1999; Leitch et al. 1997; Pagani et al. 1988; Silva, Brum, Negrao, and Krieger, 1997) or no change (Bowman et al. 1997b; Davy et al. 1997; Lightfoot, Claytor, Torok, Journell, & Fortney, 1989; Seals & Chase, 1989; Sheldahl, Ebert, Cox, & Tristani, 1994) in BRS. Some of the discrepancies of these studies may be related to methodological differences such as the technique used to assess BRS (i.e. LBNP, pharmacologic, spectral, etc.) and the duration of the training protocols, each of which will be discussed at the end of this section.

Studies using an animal model have provided evidence for a training-induced reduction in BRS. For example, in normal and sympathectomized rats, Paynter et al. reported that animals that were treadmill trained for 12 weeks (frequency: 4-6 days/week; duration: 80 minutes; intensity: 22.8 meters/min at 9% grade) demonstrated a reduced ability to maintain BP in response to graded LBNP. Tipton et al. also reported that treadmill trained rats (n=12; length: 12 weeks; frequency: 4-5 days/week; duration: 60-80 minutes; intensity: 50-75% VO_{2max}) exhibited a greater and more rapid fall in BP in response to graded LBNP than untrained controls (n=12). Similarly, Bedford and Tipton reported a blunted baroreflex in rats that were trained on a treadmill for 11-14 weeks (n=22) (frequency: 4-5 days/week; duration: 40-50 minutes; intensity: 70-90% VO_{2max}) compared to an untrained group (n=25). Following training, both groups were anesthetized and a stimulus-response curve was constructed by plotting the change in femoral artery systolic BP elicited by alterations in carotid sinus

pressure. The investigators reported a significantly flatter curve in the trained animals, with the baroreflex gain significantly lower in the trained group at pressures of 95-115 Torr (0.23 vs. 0.34) and pressures of 175-195 Torr (0.38 vs. 0.60) compared to their untrained counterparts. Additionally, Negrao et al. reported that 13 weeks of treadmill training (frequency: 5 days/week; duration: 60 minutes; intensity: 26.8 meters/minute at 15% grade) significantly attenuated BRS in rats (*n*=6) compared to nontraining controls (*n*=6). They reported a training-induced reduction in the renal sympathetic nerve activity response to a nitroprusside-induced BP decrease, and also in the HR response to a PE-induced BP increase. Both of these alterations were in the direction to suggest a reduced sensitivity of the baroreflex in the trained animals. On the other hand, in spontaneously hypertensive rats (*n*=9), Silva et al. reported that 12 weeks of treadmill training (frequency: 5 days/week; duration: 60 minutes; intensity: 50% VO_{2max}) significantly improves BRS. They reported that trained rats exhibited a significantly greater bradycardia in response to PE-induced BP increases of 8 and 15 mmHg compared to untrained controls (*n*=5). Similarly, the trained rats displayed a greater tachycardic response to BP decreases of 7, 16, and 25 mmHg induced by nitroprusside. Furthermore, the trained rats displayed a greater slope of the relationship between the changes in HR and BP in response to nitroprusside infusion. Although the data of Silva et al. suggest a training induced increase in BRS, the fact that these animals were hypertensive makes it difficult to compare these findings to other studies, as it does not reflect the response of normotensive subjects.

Studies using the human model have provided equivocal results. For example, Raven and Stevens (1990) reported that subjects (*n*=7; age=28±4 yr) who participated in an 8 month endurance training protocol (mode: walking/jogging; frequency: 4 days/week; duration: 45

minutes; intensity: 1% < ventilatory threshold) had a reduced orthostatic tolerance. Training was sufficient to increase VO_{2max} (43.9 to 56.9 ml•kg^{-1}•min^{-1}) and blood volume (6.50 to 7.25 L) and all subjects were less able to maintain BP in response to graded LBNP following training. Additionally, Stevens, Foresman, Shi, Stern, and Raven (1992) used the exact same protocol in 8 males (age=27.6±4 yr) to evaluate the influence of endurance training on orthostatic tolerance and baroreceptor function. They reported significant increases in VO_{2max} (45.2±2.0 to 57.5±3.0 ml•kg^{-1}•min^{-1}), total blood volume (15.8%), and plasma volume (16.5%), while finding a significant decreased tolerance to LBNP (-24%). They further reported that the factors accounting for reduced orthostatic tolerance were reductions in the responses of peripheral vascular resistance (R^2=0.85) and SBP (R^2=1.0) to graded LBNP, and the increase in total blood volume (R^2=0.98). Thus, these two investigations suggest that 8 months of endurance exercise training result in an attenuation of the baroreflex control of the CV system.

However, several other studies in humans have reported that endurance training has a minimal effect on BRS. For example, Lightfoot et al. (1989) used LBNP and neck pressure/suction to compare BRS between 8 males (22±1 yr) who underwent a 10-week endurance training program (mode: running/cycling; frequency: 4 days/week; duration: 20-30 minutes; intensity: 85% VO_{2max}) and a control group of 7 males of similar age (27±6 yr). Training led to an increase in VO_{2max} (46.0±2.0 to 55.0±2.0 ml•kg^{-1}•min^{-1}), while the control group exhibited no changes. Following the training period, there were no group differences in the HR, BP, or forearm blood flow response to LBNP. Similarly, there were no group differences in the HR response to changes in carotid sinus pressure induced by neck pressure/suction. In 11 older subjects (age=53±2 yr), Seals and Chase (1989) reported that 30

weeks of endurance training (mode: walk/jog; frequency: 3 days/week; duration: 30 minutes; intensity: 70% $HR_{reserve}$), which was sufficient to elicit a 25% increase in VO_{2max}, resulted in no alterations in carotid BRS, defined by the RR interval response to neck suction/pressure, relative to a control group (*n*=8; age=54±3 yr). However, they did report that training resulted in a significant reduction in the increase of forearm vascular resistance in response to graded LBNP. Sheldahl et al. (1994) studied the effect of a 12 week endurance training protocol (mode: running/cycling; frequency: 3 days/week; duration: 40 minutes; intensity: 70-85% HR_{max}) on BRS in 10 middle-aged males (54±8 yr). However, although training elicited a significant increase in VO_{2max} (30.0±2.0 to 35.0±2.0 $ml \bullet kg^{-1} \bullet min^{-1}$), the RR interval and MSNA response to either sodium nitroprusside or PE remained unchanged following training, suggesting no training-induced alterations in BRS. Davy et al. (1997) used sequence analysis to study the effects of a 12 week walking protocol (frequency: 3-4 days/week; duration: 30-45 minutes; intensity: 60-75% HR_{max}) on BRS in sedentary, hypertensive post-menopausal women (*n*=8; age=55±1 yr). They reported no training-induced difference in BRS (pre: 10±2 $ms \bullet mmHg^{-1}$; post: 13±2 $ms \bullet mmHg^{-1}$), although there was also no change in fitness level as identified by VO_{2max} (pre: 23.0±1.0 $ml \bullet kg^{-1} \bullet min^{-1}$; post: 24.0±1.0 $ml \bullet kg^{-1} \bullet min^{-1}$). Therefore, it is difficult to compare this study to others, as the training protocol was not likely intense enough to elicit any CV adaptations. In a group of older subjects (*n*=20; age=66±4 yr), Bowman et al. (1997b) examined the effect of a 6-week of endurance training protocol (mode: cycling; frequency: 2 days/week; duration; 30 minutes; intensity: 70-80% HR_{max}) on BRS, expressed by the α–index. Although the training stimulus was sufficient to increase VO_{2max} by 25%, there was no effect of training on the α–index of mid-frequency power (pre: 6.5±4;

post: 6.2±3 ms•mmHg^{-1}) or HF power (pre: 8.5±5; post: 9.9±4 ms•mmHg^{-1}), suggesting no difference in BRS.

Other studies have reported findings to suggest that endurance training significantly improves baroreflex control of the CV system. Convertino et al. (1990) examined the effect of 10 weeks of endurance training (mode: cycling; frequency: 4 days/week; duration: 30 minutes; intensity: 70-80% VO_{2max}) on the hemodynamic response to graded LBNP in previously sedentary subjects (*n*=16; age=36±1 yr) and in a nontraining, age-matched control group (*n*=8). This group reported that training significantly increased VO_{2max} (40.8 to 48.0 ml•kg^{-1}•min^{-1}), SDNN (59.4±8 to 74.0±8 ms), and blood volume (63.6±2 to 69.3±3 ml•kg^{-1}), while no similar changes were reported in the control group. They further reported no change in the carotid BRS determined by neck pressure/suction, but reported a significantly greater tolerance to LBNP (28%). With this data, they concluded that exercise endurance training significantly improves CV fitness without compromising baroreceptor function. However, they also reported a reduced slope of the linear relationship between peripheral venous pressure and forearm vascular resistance in the trained group, which would suggest a reduction in baroreflex control of vascular resistance. However, the investigators elaborated very little on this finding. Pagani et al. (1988) looked at the effect of a 6-month endurance training protocol (mode: calisthenics/jogging; frequency: 5 days/week; duration: 40 minutes; intensity: unspecified) on the BRS of 11 mildly hypertensive subjects (age=32±2 yr), expressed by both the sequence and the cross-spectral techniques. Although no measures of fitness were reported as an indication of CV adaptations elicited by the protocol, the authors reported that training resulted in a significant elevation of the slope of the RR-SBP relationship during a PE-induced pressure increase (14.7±2 vs. 19.5±3 ms•mmHg^{-1}).

Furthermore, they reported an increase in BRS expressed by the α-indices in both the LF (10.4±1 vs. 15.4±3 ms•mmHg^{-1}) and HF (12.2±1 vs. 21.5±3 ms•mmHg^{-1}) power ranges. Grassi et al. (1994) studied the effects of a 10-week endurance training protocol (mode: running; frequency: 5 days/week; duration: 2 hours) on the HR and MSNA responses to PE-induced increases and nitroprusside-induced decreases in BP in a group of 9 previously sedentary subjects (age=16±1 yr). Training resulted in an 18% increase in VO_{2max}, and further resulted in a greater reduction in the HR and MSNA response to PE-induced increases in BP (-8.6±1 vs. –6.1±1 beats/minute and -78±5 vs. -54±5%, respectively). Similarly, training resulted in greater increases in HR and MSNA in response to nitroprusside-induced decreases in BP (18.6±3 vs. 12.4±2 beats/minute and 128.1±26 vs. 63.2±11%, respectively). Additionally, there were no alterations in any of these parameters in a group of 4 age-matched control subjects that were measured simultaneously. Guo et al. (1999) assessed BRS, expressed by the slope of the change in RR interval to that of SBP during the Valsalva maneuver, before, during, and after a 6-month training protocol (mode: various; frequency: 3 days/week; duration: total of 2.5 hr/week; intensity: "mild"). Although there were no differences in baseline values between the subjects who underwent this training program (*n*=20; age=41±8 yr) and a control group (*n*=10; age=39±8 yr), the training group exhibited an increased BRS at 3 (+92%) and 6 months (+169%), while BRS was unaltered in the controls. Lastly, in a previously mentioned study of patients with a recent myocardial infarction (n=26; age=56±1 yr), Leitch et al. (1997) examined the influence of a 6-week training protocol (mode: cycling; frequency: 3-4 days/week; duration: 30-60 minutes; intensity: 70% HR_{max}) on BRS, estimated by the sequence technique. In response to PE infusion, they were able to show a greater increase in BRS compared to a control group of

similar health status (*n*=23; age=59±1 yr), who participated only in a home-based walking program (+3.4±1 vs. +1.7±1 ms•mmHg^{-1}).

Although the results of these studies evaluating the influence of endurance training on BRS appear to be inconclusive, a few factors must be considered in these investigations. For instance, the majority of training protocols have been less than 6 months in duration. Therefore, it is possible that several of the studies that found no differences in BRS following training did not allow for a complete adaptation of the baroreceptors. Although most were sufficient in length to significantly improve VO_{2max}, it is possible that fitness, per se, is not related to BRS. It may be that other CV adaptations that occur over longer periods of training are responsible for some of the differences in BRS between chronically trained endurance athletes and sedentary individuals that were previously mentioned. Thus, the studies that have involved longer periods of training (>6 months) may be more valid. Another factor that demands consideration when examining these studies is the technique used to assess BRS. As mentioned earlier, LBNP results in both a central hypovolemia and hypotension which likely stimuates both the arterial and cardiopulmonary baroreceptors. Conversely, neck pressure/suction primarily activates the carotid baroreflex. Additionally, the sequence and cross-spectral techniques do not differentiate between different populations of baroreceptors. Thus, one must carefully critique the methodology used in evaluating BRS, as it is very possible that endurance training has differential effects on each.

Looking specifically at those studies with training periods greater than 6 months, those that used LBNP suggest an attenuated BRS (Raven & Stevens, 1990; Seals & Chase, 1989; Stevens et al. 1992). Furthermore, Seals and Chase found no differences in carotid BRS, therefore suggesting an attenuation of the aortic and/or cardiopulmonary baroreflex. One

possible mechanism that may play a role in altering BRS is blood volume, although this variable was reported only in a small portion of investigations. Although blood volume may increase significantly over short periods of exercise training, it is possible that chronically elevated blood volume results in alterations of BRS that occur over a time course of months to years. A slight elevation in blood volume would have a direct impact on the baroreceptors, namely the aortic. A continuous pumping of an increased blood volume through the aortic arch may lead to a loss in sensitivity of the aortic baroreflex. Methodological differences may also partially explain the findings of Pagani et al. (1988) and Guo et al. (1999) who used the cross-spectral and sequence techniques, respectively, and reported a training-induced increase in BRS. If the findings of these investigators were a result of increased cardiopulmonary baroreceptor sensitivity, it may be that the arterial baroreflex was actually reduced, as increased cardiopulmonary baroreceptor activation has been demonstrated to reduce arterial BRS (Billman et al. 1981). This then would fit nicely with the data of investigators reporting reduced BRS (Raven & Stevens; Seals & Chase; Stevens et al. 1992), However, these hypotheses are purely speculatory, and more longitudinal research should be initiated on this subject matter.

Studies assessing muscle sympathetic nerve activity. There exist few longitudinal studies that have examined the influence of exercise endurance training on MSNA. Svedenhag et al. (1984) was the first to study the effects of an endurance training protocol on MSNA. In 5 untrained subjects (age=23.6±1 yr), they reported that 8 weeks of cycling at an intensity of 75% VO_{2max} (frequency: 4 days/week; duration: 40 minutes) did not significantly alter resting MSNA expressed as either bursts/min (pre: 24±5; post: 23±4) or bursts/100 heart beats (pre: 38±9; post: 39±7). However, although the training stimulus elicited a significant increase in

VO_{2max}, the change was relatively small (~7%), therefore leading to the possibility that the stimulus may have not been sufficient to alter MSNA. Still, Sheldahl et al. (1994) reported similar findings following a 12-week training protocol (mode: running/cycling; frequency: 3 days/week; duration: 40 minutes; intensity: 70-85% HR_{max}) in 10 males (age=54±8 yr). In this study, training resulted in an increase in VO_{2max} (~17%), but there was no change in resting MSNA (23.4±2 vs. 23.6±2 bursts/min). Additionally, they found no training-related changes in the MSNA response to 3 minutes of isometric handgrip exercise at 25 % MVC (6.8±2 vs. 4.7±3), the cold pressor test (6.1±3 vs. 8.3±3), or 7 degree head-up tilt (2.1±2 vs. 0.8±2). Additionally, in a study presented in an abstract, Ray, Pace, and Clary (1992) reported no change in resting MSNA following 6 weeks of one-legged training on a cycle ergometer (frequency: 4 days/week; duration: 40 minutes; intensity: 70% VO_{2peak}) in 5 males (age=19-23 yr) relative to a control group (*n*=5) within the same age range. However, the VO_{2peak} of the trained leg reportedly increased by 20%. Conversely, Grassi, Seravalle, Calhoun, and Mancia (1994) reported that a 10-week running protocol (frequency: 5 days/week; duration: 2 hours) significantly increased VO_{2max} (16%) and decreased resting MSNA (21 vs. 14 bursts/min) in a group of 9 subjects (age=17±1 yr) compared to a control group consisting of 4 subjects (24 vs. 23 bursts/min). The results of these longitudinal studies are obviously inconclusive, with most suggesting that MSNA is unaffected by exercise endurance training. However, these studies are limited by the length of there training protocols. It may be that longer training protocols (>12-weeks) that elicit greater improvements in CV fitness may provide different results. Nevertheless, more longitudinal studies need to be performed before definite conclusions can be drawn.

Summary. In conclusion, there is evidence to suggest a significant effect of endurance exercise training on autonomic regulation of the CV system. Studies using HRV have reported a shift towards increased vagal control of HR in as little as 6 weeks of training in healthy and as little as 2 weeks of training in diseased populations. Regarding the effects of training on plasma catecholamines, it appears as though exercise training reduces the catecholamine response to exercise at the same absolute workload, while the effect of training on the catecholamine response to exercise at a given percentage of VO_{2max} remains debatable. Additionally, the effect of training on resting catecholamine concentration and the catecholamine response to a psychological challenge are not well established. Studies examining the influence of training on the CV response to stress have provided mixed results, although it appears that those studies that have used training protocols greater than 12 weeks and/or those that have studied subjects with some pre-existing condition have shown the most promise. Similarly, the influence of training on BRS is not well established, although it is possible that it may require extended periods of training to elicit changes in baroreceptors function. Furthermore, it is likely that different populations of baroreceptors do not respond in a similar fashion to exercise training. Lastly, few studies have looked specifically at the influence of training on MSNA and are not conclusive.

Summary and Conclusions

The CV system is tightly regulated by the ANS in order to maintain homeostasis and to respond to constant physiological challenges. The ANS allows the CV system to respond favorably to these challenges by regulating cardiac and vascular tone quickly and efficiently. Autonomic outflow is controlled by the brain stem, spinal cord, portions of the cerebral cortex, hypothalamus, and by reflex mechanisms that transmit information to these control

centers. The two components of the ANS, the SNS and PNS, have preganglionic nerve fibers that transmit impulses that exit the CNS and synapse with postganglionic fibers in the periphery that relay the impulses to target organs. Subsequently, the response that occurs at a target organ is dependent on both the type and concentration of its receptors.

Several techniques have been developed to evaluate autonomic function. These include the variability of HR and BP, examination of plasma catecholamines, MSNA, SSR, CV reactivity, and BRS. The use of these techniques, along with a few others, has allowed investigators to make inferences about autonomic modulation under various conditions and furthermore, about the effect of longitudinal interventions on the ANS. Additionally, there are several factors that can influence autonomic activity, and thus, must be controlled for during experimental conditions. These include, but are not limited to, age, race, gender, and environmental influences such as temperature and altitude. Other factors, not included in this review include personality type and the presence of various diseases.

An acute bout of rhythmic exercise involving large muscle groups is associated with changes in autonomic regulation of the CV system. In general, there is a withdrawal of vagal efferent activity at the onset of an acute bout of rhythmic exercise. The immediate reduction in cardiac vagal modulation is likely mediated via central command due to the rapidity at which this vagal withdrawal occurs. However, it there is other data to suggest that an immediate resetting of the arterial baroreflex can result in an error signal also eliciting a vagal withdrawal. Subsequently, as exercise intensity increases there is a gradual increase in sympathetic outflow mediated by further baroreflex resetting and muscle mechano- and metaboreceptors.

Many studies have examined the relationship between peak aerobic power and autonomic regulation of the CV system. Those investigations that have used CV reactivity as an indicator of autonomic integrity have provided mixed results. Many of these discrepancies are possibly the result of the use of different classifications of physical fitness and different methods of evaluating fitness. Furthermore, many of these studies did not control for initial group differences in CV reactivity or did adjust for initial differences when they were not present. Nevertheless, although investigators have extensively examined the relationship between aerobic power and CV reactivity, there is still little consensus in the literature. Thus, it is likely that CV reactivity is not sensitive enough to detect autonomic differences in subjects of varying fitness levels. Investigators searching for a relationship between fitness and resting plasma catecholamines have failed to find such a relationship. However, studies have shown that there is an attenuated NE response to exercise at identical submaximal workloads in high- compared to lower-fit subjects. Conversely, there is no consensus on the influence of fitness on the catecholamine response to exercise at the same relative intensity. Additionally, those studies that have reported high-fit subjects exhibit attenuated NE reactivity to psychological stimuli have used control groups with very low levels of physical fitness, while those using control groups of moderate-to-high fitness levels have shown no such association. On the other hand, the E response to psychological stimuli does not appear to be related to aerobic power. Studies that have used HRV to examine the relationship between fitness and autonomic activity have provided evidence for a strong positive relationship. Both time and spectral indices of HRV have been significantly correlated with aerobic power, suggesting that high levels of fitness are associated with an enhanced vagal modulation of the heart. Thus, this measure appears to be sensitive to fitness-related

differences in cardiac autonomic regulation. Additionally, several investigators have searched for an association between BRS and physical fitness. Although these data are somewhat controversial, it appears as though the aortic baroreflex is most influenced by fitness level, while the carotid and cardiopulmonary baroreceptors are not greatly affected. Alternatively, only a few studies have examined the influence of aerobic power on MSNA and there is no general consensus on this matter.

Endurance exercise training results in several CV adaptations that may be accounted for, in part, by changes in autonomic regulation. Studies that have used CV reactivity as an index of autonomic control have provided mixed results regarding an influence on training on ANS function. However, it appears as though most studies that used subjects with a pre-existing condition (e.g. type-A personality, hypertension) showed a beneficial effect of training on CV reactivity. Additionally, the majority of studies that used training protocols greater than 12 weeks in length showed an attenuation of CV reactivity, although a few studies have found improvements with protocols of shorter durations. Those investigations that have examined the influence of exercise training on resting plasma catecholamines have been inconclusive with some reporting a reduction and others reporting no effect. Therefore, it is possible that the catecholamine response to physiological perturbations may be a more sensitive measure of ANS activity. Accordingly, investigators have reported that the catecholamine response to exercise at a given workload is lower following participation in an endurance training protocol. Alternatively, the influence of exercise training on the catecholamine response to exercise at a percentage of one's VO_{2max} is still unclear, although several studies have reported an increased catecholamine response following training. Furthermore, studies have reported no effect of exercise training on the catecholamine

response to psychological stimuli. Several investigators using HRV have reported an enhanced cardiac vagal modulation following an exercise training protocol in both healthy and diseased populations. Research still remains controversial regarding the influence of exercise training on BRS. Animal models have provided evidence for a reduced BRS following a training protocol. However, studies in humans have provided inconclusive results. Differences in the findings of these studies are possibly the result of different techniques of measurement and/or differences in the length of the training protocols. Additionally, it is possible that it requires extended periods of training (longer than any longitudinal study to date) to elicit pronounced alterations in BRS. Lastly, the majority of investigations have found no influence of exercise training on resting MSNA.

Although there has been an extensive amount of research regarding the influence of peak aerobic power and endurance exercise training on autonomic control of the CV system, there still remain several areas that warrant further investigation. For example, although several studies have reported that exercise training influences autonomic control of the circulation, the time course of these changes remains elusive. It would be of interest to the scientific and medical fields to elucidate the chronology of such alterations. If a training threshold could be identified at which autonomic alterations take place, it may greatly impact the manner in which exercise training is prescribed to both healthy and diseased populations. Additionally, although several investigations have addressed the influence of fitness and exercise training on BRS in healthy young and older adults, no study has looked at this relationship in an African American population. Since this population has a greater incidence of hypertension relative to Caucasians, it would be of interest to see if their baroreceptors are affected differentially.

In conclusion, it appears that both peak aerobic power and endurance exercise training influence autonomic control of the CV system. Additionally, some techniques appear to be more sensitive than others in demonstrating relationships between these variables. Furthermore, the extent to which peak aerobic power influences autonomic control appears to be related the factors including the technique used to assess peak aerobic power and the range of fitness levels of the subjects examined, while the extent to which exercise training influences autonomic regulation appears to be related to the specifics of the training protocol (i.e. length, mode, frequency, intensity, duration).

References

Abrass, I.B., Davis, J.L., & Scarpace, P.J. (1982). Isoproterenol responsiveness and myocardial beta-adrenergic receptors in young and old rats. Journal of Gerontology, 37, 156-160.

Akselrod, S. (1995). Components of heart rate variability – basic studies. In M. Malik and A.J. Camm (Eds.), Heart Rate Variability. (pp.147-163). Armonk, New York: Futura.

Akselrod, S., Gordon, D., Ubel, F.A., Shannon, D.C., Barger, A.C., & Cohen, R.J. (1981). Power spectrum analysis of heart rate fluctuations: a quantitative probe of beat-to-beat cardiovascular control. Science, 213, 220-222.

Akselrod, S., Gordon, D., Madwed, J.B., Snidman, N.C., Shannon, D.C., & Cohen, R.J. (1985). Hemodynamic regulation: investigation by spectral analysis. American Journal of Physiology, 249, H867-H875.

Al-Ani, M., Munir, S.M., White, M., Townend, J., & Coote, J.H. (1996). Changes in R-R variability before and after endurance training measured by power spectral analysis and by the effect of isometric muscle contraction. European Journal of Applied Physiology, 74, 397-403.

Alam, M., & Smirk, F.H. (1937). Observations in man upon a blood pressure raising reflex arising from the voluntary muscles. Journal of Physiology, 89, 372-383.

Arai, Y., Saul, J.P., Albrecht, P., Hartley, L.H., Lilly, L.S., Cohen, R.J., & Colucci, W.S. (1989). Modulation of cardiac autonomic activity during and immediately after exercise. American Journal of Physiology, 256, H132-H141.

Armstrong, D.W. (1998). Metabolic and endocrine responses to cold air in women differing in aerobic capacity. Medicine and Science in Sports and Exercise, 30, 880-884.

Baba, M., Watahiki, Y., Matsunaga, M., & Takebe, K. (1988). Sympathetic skin response in healthy man. Electromyography and Clinical Neurophysiology, 28, 277-283.

Barnett, S.R., Morin, R.J., Kiely, D.K., Gagnon, M., Azhar, G., Knight, E.L., Nelson, J.C., & Lipsitz, L.A. (1999). Effects of age and gender on autonomic control of blood pressure dynamics. Hypertension, 33, 1195-1200.

Barney, J.A., Ebert, T.J., Groban, L., Farrell, P.A., Hughes, C.V., & Smith, J.J. (1988). Carotid baroreflex responsiveness in high-fit and sedentary young men. Journal of Applied Physiology, 65, 190-194.

Bedford, T.G. & Tipton, C.M. (1987). Exercise training and the arterial baroreflex. Journal of Applied Physiology, 63, 1926-1932.

Bernardi, L., Passino, C., Spadacini, G., Calciati, A., Robergs, R., Greene, R., Martignoni, E., Anand, I., & Appenzeller, O. (1998). Cardiovascular autonomic modulation and activity of carotid baroreceptors at altitude. Clinical Science, 95, 565-573.

Bernardi, L., Salvucci, F., Suardi, R., Solda, P.L., Calciati, A., Perlini, S., Falcone, C. & Ricciardi, L. (1990). Evidence for an intrinsic mechanism regulating heart rate variability in the transplanted and the intact heart during submaximal exercise? Cardiovascular Research, 24, 969-981.

Bevegard, B.S., & Shepard, J.T. (1966). Circulatory effects of stimulating the carotid arterial stretch receptors in man at rest and during exercise. Journal of Clinical Investigation, 45, 132-142.

Bigger, J.T., Fleiss, J.L., Rolnitzky, L.M., & Steinman, R.C. (1992). Stability over time of heart period variability in patients with previous myocardial infarction and ventricular arrhythmias. American Journal of Cardiology, 89, 718-723.

Billman, G.E., Dickey, D.T., Teoh, K.K., & Stone, H.L. (1981). Effects of central venous blood volume shifts on arterial baroreflex control of heart rate. American Journal of Physiology, 241, H571-H575.

Billman, G.E., Schwartz, P.J., & Stone, H.L. (1982). Baroreceptor reflex control of heart rate: A predictor of sudden cardiac death. Circulation, 66, 874-880.

Bini, G., Hagbarth, K.E., Hynninen, P., & Wallin, B.G. (1980). Thermoregulatory and rhythm-generating mechanisms governing the sudomotor and vasoconstrictor outflow in human cutaneous nerves. Journal of Physiology, 306, 537-552.

Bland, J.M., & Altman, D.G. (1986). Statistical methods for assessing agreement between two methods of clinical measurement. Lancet, 2, 307-310.

Bloom, S., Johnson, R., Park, D., Rennie, M., & Sulaiman, W. (1976). Differences in the metabolic response to exercise between racing cyclists and untrained individuals. Journal of Physiology, 258, 1-18.

Blumenthal, J.A., Emery, C.F., Walsh, M.A., Cox, D.R., Kuhn, C.M., Williams, R.B., & Williams, R.S. (1988). Exercise training in healthy type A middle-aged men: effects on behavioral and cardiovascular responses. Psychosomatic Medicine, 50, 418-433.

Blumental, J.A., Fredrickson, M., Kuhn, C.M., Ulmer, R.L., Walsh-Riddle, M., & Appelbaum, M. (1990). Aerobic exercise reduces levels of cardiovascular and sympathoadrenal responses to mental stress in subjects without prior evidence of myocardial ischemia. American Journal of Cardiology, 65, 93-98.

Bonaduce, D., Petretta, M., Cavallaro, V., Apicella, C., Ianniciello, A., Romano, M., Breglio, R., & Marciano, F. (1998). Intensive training and cardiac autonomic control in high level athletes. Medicine and Science in Sports and Exercise, 30, 691-696.

Bond, V., Mills, R.M., Caprarola, M., Vaccaro, P., Adams, R.G., Blakely, R., Roltsch, M., Hatfield, B., Davis, G.C., Franks, B.D., Fairfax, J., & Banks, M. (1999). Aerobic exercise attenuates blood pressure reactivity to cold pressor test in normotensive, young adult African-American women. Ethnicity and Disease, 9, 104-110.

Boutcher S.H., Nugent, F.W., McLaren, P.F., & Weltman, A.L. (1998). Heart period variability of trained and untrained men at rest and during mental challenge. Psychophysiology, 35, 16-22.

Boutcher, S.H., & Stein, P. (1995). Association between heart rate variability and training response in sedentary middle-aged men. European Journal of Applied Physiology, 70, 75-80.

Bowman, A.J., Clayton, R.H., Murray, A., Reed, J.W., Subhan, M.F., & Ford, G.A. (1997). Baroreflex function in sedentary and endurance-trained elderly people. Age and Ageing, 26, 289-294.

Braun, L.T., Potempa, K., Holm, K., Fogg, L., & Szidon, J.P. (1994). The role of catecholamines, age, and fitness on blood pressure reactivity to dynamic exercise in patients with essential hypertension. Heart and Lung, 23, 404-412.

Brenner, I.K.M., Thomas, S., & Shepard, R.J. (1997). Spectral analysis of heart rate variability during heat exposure and repeated exercise. European Journal of Applied Physiology, 76, 145-156.

Breuer, H.W.M., Skyschally, A., Schulz, R., Martin, C., Wehr, M., & Heusch, G. (1993). Heart rate variability and circulating catecholamine concentrations during steady state exercise in healthy volunteers. British Heart Journal, 70, 144-149.

Brooke, S.T., & Long, B.C. (1987). Efficiency of coping with a real-life stressor: a multimodal comparison of aerobic fitness. Psychophysiology, 24, 173-180.

Brooks, G.A., Fahey, T.D., & White, T.P. (1995). Exercise Physiology: Human Bioenergetics and its applications. Mountain View: Mayfield Publishing Company.

Brundin, T., & Cernigliaro, C. (1975). The effect of physical training on the sympathoadrenal response to exercise. Scandinavian Journal of Clinical and Laboratory Investigation, 35, 525-530.

Burger, A.J., Charlamb, M., Weinrauch, L.A., & D'Elia, J.A. (1997). Short- and long-term reproducibility of heart rate variability in patients with long-standing type-I diabetes mellitus. American Journal of Cardiology, 80, 1198-1202.

Calvelo, M.G., Abboud, F.M., Ballard, D.R., & Abdel-Sayed, W. (1970). Reflex vascular responses to stimulation of chemoreceptors with nicotine and cyanide: activation of adrenergic constriction in muscle and noncholinergic dilation in dog's paw. Circulation Research, 27, 259-276.

Casadei, B., Cochrane, S., Johnston, J. Conway, J. & Sleight, P. (1995). Pitfalls in the interpretation of spectral analysis of the heart rate variability during exercise in humans. Acta Physiologica Scandinavica, 153, 125-31.

Chevalier, B., Mansier, P., Teiger, E., Callens-El Amrani, F., & Swynghedauw, B. (1991). Alterations in adrenergic and muscarinic receptors in aged rat heart. Effects of chronic administration of propranolol and atropine. Mechanisms of Ageing and Development, 60, 215-224.

Christensen, N.J., & Brandsborg, O. (1973). The relationship between plasma catecholamine concentration and pulse rate during exercise and standing. European Journal of Clinical Investigation, 3, 299-306.

Clausen, J.P. (1977). Effects of physical training on cardiovascular adjustment to exercise. Physiological Reviews, 57, 779-815.

Claytor, R., Cox, R., Howley, E., Lawler, K., & Lawler, J. (1988). Aerobic power and cardiovascular response to stress. Journal of Applied Physiology, 65, 1416-1423.

Cleroux, J., Peronnet, F., & de Champlain, J. (1987). Effects of exercise training on plasma catecholamines and blood pressure in labile hypertensive subjects. European Journal of Applied Physiology, 56, 550-554.

Cleroux, J., Peronnet, F., & de Champlain, J. (1985). Sympathetic indices during psychosocial and physical stimuli before and after training. Physiology and Behavior, 35, 271-275.

Coats, A.J.S., Adamopoulas, S., Radaelli, A., McCance, A., Meyer, T.E., Bernardi, L., Solda, P.L., Davey, P., Ormerod, O., Forfar, C., Conway, J., & Sleight, P. (1992). Controlled trial of physical training in chronic heart failure: exercise performance, hemodynamics, ventilation, and autonomic function. Circulation, 85, 2119-2131.

Convertino, V.A., Mathes, K.L., Lasley, M.L., Tomaselli, C.M., Frey, M.A.B., & Hoffler, G.W. (1993). Hemodynamic and hormaonal responses to lower body negative pressure in men with varying profiles of strength and aerobic power. European Journal of Applied Physiology, 67, 492-498.

Convertino, V.A., Thompson, C.A., Eckberg, D.L., Fritsch, J.M., Mack, J.W., & Nadel, E.R. (1990). Baroreflex responses and LBNP tolerance following exercise training. The Physiologist, 33, s40-s41.

Conway, J., Wheeler, R., & Sannerstedt, R. (1971). Sympathetic nervous activity during exercise in relation to age. Cardiovascular Research, 5, 577-581.

Cooksey, J.D., Reilly, P., Brown, S., Bomze, H., & Cryer, P.E. (1978). Exercise training and plasma catecholamines in patients with ischemic heart disease. American Journal of Cardiology, 42, 372-376.

Cousineau, D., Ferguson, R.J., De Champlain, J., Gauthier, P., Cote, P., & Bourassa, M. (1977). Catecholamines in coronary sinus during exercise in man before and after training. Journal of Applied Physiology, 43, 801-806.

Cox, R.H. (1991). Exercise training and response to stress: insights from an animal model. Medicine and Science in Sports and Exercise, 23, 853-859.

Czajkowski, S.M., Hindelang, R.D., Dembroski, T.M., Mayerson, S.E., Parks, E.B., & Holland, J.C. (1990). Aerobic fitness, psychological characteristics, and cardiovascular reactivity to stress. Health Psychology, 9, 676-692.

D'Alpa, F., Scandurra, L., Lanaia, F., Scrofani, A., & Grasso, A. (1988). Sympathetic skin response in chronic renal failure. Acta Neurologica, 10, 280-285.

Daly, M., & Kirkman, E. (1989). Differential modulation by pulmonary stretch receptor afferents of some reflex cardioinhibitory responses in the cat. Journal of Physiology, 417, 323-342.

Daly, M., & Scott, M.J. (1958). The effects of stimulation of the carotid body chemoreceptors on heart rate in the dog. Journal of Physiology, 144, 148-166.

Daly, M., & Scott, M.J. (1962). An analysis of the primary cardiovascular reflex effects of stimulation of the carotid body chemoreceptors in the dog. Journal of Physiology, 162, 555-573.

Daly, M., & Scott, M.J. (1963). The cardiovascular responses to stimulation of the carotid body chemoreceptors in the dog. Journal of Physiology, 165, 179-197.

Davy, K.P., DeSouza, C.A., Jones, P.P., & Seals, D.R. (1998). Elevated heart rate variability in physically active young and older adult women. Clinical Science, 94, 579-584.

Davy, K.P., Willis, W., & Seals, D.R. (1997). Influence of exercise training on heart rate variability in post-menopausal women with elevated arterial blood pressure. Clinical Physiology, 17, 31-40.

Dawson, S.L., Robinson, T.G., Youde, J.H., James, M.A., Martin, A., Weston, P., Paneral, R., & Potter, J.F. (1997). The reproducibility of cardiac baroreceptor activity assessed non-invasively by spectral and sequence techniques. Clinical Autonomic Research, 7, 279-284.

De Ferrari, G.M., Vanoli, E., Stramba-Badiale, M., Hull, S.S. Jr., Foreman, R.D., & Schwartz, P.J. (1991). Vagal reflexes and survival during acute myocardial ischemia in conscious dogs with healed myocardial infarction. American Journal of Physiology, 261, H63-H69.

De Geest, H., Levy, M., & Zieske, H. (1965). Carotid chemoreceptor stimulation and ventricular performance. American Journal of Physiology, 209, 564-570.

De Geus, E.J., Van Doornen, L.J., & Orlebeke, J.F. (1993). Regular exercise and aerobic fitness in relation to psychological make-up and physiological stress reactivity. Psychosomatic Medicine, 55, 347-363.

De Geus, E.J., Van Doornen, L.J., De Visser, D.C., & Orlebeke, J.F. (1990). Existing and training induced differences in aerobic fitness: their relationship to physiological response patterns during different types of stress. Psychophysiology, 27, 457-478.

Deligiannis, A., Kouidi, E., & Tourkantonis, A. (1999). Effects of physical training on heart rate variability in patients on hemodialysis. American Journal of Cardiology, 84, 197-202.

Del Rio, G., Velardo, A., Zizzo, G., Avogardo, A., Cipolli, C., Della Casa, L., Marrama, P., & Macdonald, I.A. (1994). Effect of estradiol on the sympathoadrenal response to mental stress in normal men. Journal of Clinical Endocrinology and Metabolism, 79, 836-840.

De Meersman, R.E. (1992). Respiratory sinus arrhythmia alteration following training in endurance athletes. European Journal of Applied Physiology, 64, 434-436.

De Meersman, R.E. (1993). Heart rate variability and aerobic fitness. American Heart Journal, 125, 726-731.

DiCarlo, S.E., & Bishop, V.S. (1992). Onset of exercise shifts operating point of arterial baroreflex to higher pressures. American Journal of Physiology, 262, H303-H307.

Dimier-David, L., Billon, N., Costagliola, D., Jaillon, P., & Funck-Brentano, C. (1994). Reproducibility of non-invasive measurement and of short-term variability of blood pressure and heart rate in healthy volunteers. British Journal of Clinical Pharmacology, 38, 109-115.

Dixon, E.M., Kamath, M.V., McCartney, N., & Fallen, E.L. (1992). Neural regulation of heart rate variability in endurance athletes and sedentary controls. Cardiovascular Research, 26, 713-719.

Donald, D.E., & Edis, A.J. (1971). Comparison of aortic and carotid baroreflexes in the dog. Journal of Physiology, 215, 521-538.

Dorheim, T.A., Ruddel, J.C., & Eliot, R.S. (1984). Cardiovascular response of marathoners to mental challenge. Journal of Cardiac Rehabilitation, 4, 476-480.

Duncan, J., Farr, J., Upton, J., Hagen, R., Oglesby, M., & Blair, S. (1985). The effects of aerobic exercise on plasma catecholamines and blood pressure in patients with mild hypertension. Journal of the American Medical Association, 254, 2609-2613.

Echt, M., Duweling, J., Gauer, O.H., & Lange, L. (1974). Effective compliance of the total vascular bed and the intrathoracic compartment derived from changes in central venous pressure induced by volume changes in man. Circulation Research, 40, 61-68.

Eckberg, D.L., Convertino, V.A., Fritsch, J.M., & Doerr, D.F. (1992). Reproducibility of human vagal carotid baroreceptor-cardiac reflex responses. American Journal of Physiology, 263, R215-R220.

Edis, A.J., Donald, D.E., & Shepher, J.T. (1970). Cardiovascular reflexes from stretch of pulmonary vein-atrial junctions in the dog. Circulation Research, 27, 1091-1100.

Ehsani, A.A., Heath, G.W., Martin, W.H., Hagberg, J.M., & Holloszy, J.O. (1984). Effects of intense exercise training on plasma catecholamine levels in coronary patients. Journal of Applied Physiology, 57, 154-159.

Ekblom, B. (1968). Effect of physical training on oxygen transport system in man. Acta Physiologica Scandinavica, 328, 1-45.

Ekblom, B., Goldbarg, A.N., Kilbom, A., & Astrand, P.O. (1972). Effects of atropine and propranolol on the oxygen transport system during exercise in man. Scandinavian Journal of Clinical Laboratory Investigation, 30, 35-42.

Eldridge, F.L., Millhorn, D.E., Kiley, J.P., & Waldrop, T.G. (1985). Stimulation by central command of locomotion, respiration, and circulation during exercise. Respiratory Physiology, 59, 313-337.

Esler, M. (1982). Assessment of sympathetic nervous system function in humans from noradrenaline plasma kinetics. Clinical Science, 62, 247-254.

Esler, M., Jennings, G., Korner, P., Willet, I., Dudley, F., Hasking, G., Anderson, W., & Lambert, G. (1988). Assessment of human sympathetic nervous system activity from measurements of norepinephrine turnover. Hypertension, 11, 3-20.
Esler, M., Jennings, G., Lambert, G., Meredith, I., Horne, M., & Eisenhofer, G. (1990). Overflow of catecholamine neurotransmitters to the circulation: source, fate, and functions. Physiological Reviews, 70, 963-985.

Ewing, D.J., Neilson, J.M.M., Shapiro, C.M., Stewart, J.A., & Reid, W. (1991). Twenty-four hour heart rate variability: effects of posture, sleep, and time of the day in healthy controls and comparison with bedside tests of autonomic function in diabetic patients. British Heart Journal, 65, 239-244.

Fagius, J., & Wallin, B.G. (1983). Microneurographic evidence of excessive sympathetic outflow in the Guillain-Barre syndrome. Brain, 106, 589-600.

Fagius, J., & Wallin, B.G. (1993). Long-term variability and reproducibility of resting human muscle nerve sympathetic activity at rest, as reassessed after a decade. Clinical Autonomic Research, 3, 201-205.

Fagraeus, L., & Linnarsson, D. (1976). Autonomic origin of heart rate fluctuations at the onset of muscular exercise. Journal of Applied Physiology, 40, 679-682.

Featherstone, J.A., Veith, R.C., Flatness, D., Murburg, M.M., Villacres, E.C., & Halter, J.B. (1987). Age and alpha-2 adrenergic regulation of plasma norepinephrine kinetics in humans. Journal of Gerontology, 42, 271-276.

Fidone, S.J., & Gonzales, C. (1986). Initiation and control of chemoreceptor activity in the carotid body. In A.P. Fishman, N.S. Cherniak, J.G. Widdicombe, & S.R. Gieger. (Eds.) American Physiological Society Handbook of Physiology; Section III; The Respiratory System; Volume II; Part I; The Control of Breathing (pp. 247-312). London: Oxford University Press.

Fiocchi, R., Fagard, R., Vanhees, L., Grauwels, R., & Amery, A. (1985). Carotid baroreflex sensitivity and physical fitness in cycling tourists. European Journal of Applied Physiology, 54, 461-465.

Fleg, J.L., Gerstenblith, G., Schulman, S.P., Becker, L.C., O'Conner, F.C. & Lakatta, E.G. (1990). Gender differences in exercise hemodynamics of older subjects: effects of conditioning status (Abstract). Circulation, 82, (Suppl. III), III-239.

Fleg, J.L., Schulman, S.P., O'Conner, F.C., Gerstenblith, G., Clulow, J.F., Renlund, D.G., & Lakatta, E.G. (1991). Effect of propranolol on age-associated changes in left ventricular performance during exercise (Abstract). Circulation, 84, (Suppl. II), II-187.

Fleg, J.L., Tzankoff, S.P., & Lakatta, E.G. (1985). Age-related augmentation of plasma catecholamines during dynamic exercise in healthy males. Journal of Applied Physiology, 59, 1033-1039.

Folkow, B. (1982). Physiological aspects of primary hypertension. Physiological Reviews, 62, 347-503.

Fortney, S., Tankersley, C., Lightfoot, J.T., Drinkwater, D., Clulow, J., Gerstenblith, G., O'Conner, F., Becker, L., Lakatta, E., & Fleg, J. (1992). Journal of Applied Physiology, 73, 2693-2700.

Franz, D.N., & Iggo, A. (1968). Conduction failure in myelinated and non-myelinated axons at low temperatures. Journal of Physiology, 199, 319-345.

Freed, L.A., Stein, K.M., Gordon, M., Urban, M., & Kligfield, P. (1994). Reproducibility of power spectral measures of heart rate variability obtained from short sampling periods. American Journal of Cardiology, 74, 972-973.

Freund, P.R., Hobbs, S.F., & Rowell, L.B. (1978). Cardiovascular responses to muscle ischemia in man-dependency on muscle mass. Journal of Applied Physiology, 45, 762-767.

Froklis, V.V., Bezrukov, V.V., & Schevtchuk, V.G. (1975). Hemodynamics and its regulation in old age. Experimental Gerontology, 10, 251-271.

Froklis, V.V., Bezrukov, V.V., Bogatskaya, L.N., Verkhratsky, N.S., Zamostian, V.P., Shevtchuk, V.G., & Shtchegoleva, I.V. (1979). Catecholamines in the metabolism and functions regulation in aging. Gerontologia, 16, 129-140.

Fujimoto, S., Uemura, S., Tomoda, Y., Yamamoto, H., Matsukura, Y., Horii, M., Iwamoto, E., Hashimoto, T., & Dohi, K. (1999). Effects of exercise training on the heart rate variability and QT dispersion of patients with acute myocardial infarction. Japanese Circulation Journal, 63, 577-582.

Furedy, J.J., & Heslegrave, R.J. (1983). A consideration of recent criticism of the T-wave amplitude index of myocardial sympathetic activity. Psychophysiology, 20, 204-211.

Furlan, R., Piazza, S., & Dell'Orto, S. (1993). Early and late effects of exercise and athletic trainng on neural mechanisms controlling heart rate. Cardiovascular Research, 27, 482-488.

Gallagher, D., Terenzi, T., & De Meersman, R. (1992). Heart rate variability in smokers, sedentary and aerobically fit individuals. Clinical Autonomic Research, 2, 383-387.

Gerin, W., Rosofsky, M., Pieper, C., & Pickering, T.G. (1993). A test of reproducibility of blood pressure and heart rate variability using a controlled ambulatory procedure. Journal of Hypertension, 11, 1127-1131.

Gillum, R.F. (1979). Pathophysiology of hypertension in blacks and whites. Hypertension, 1, 468-475.

Goldsmith, R.L., Bigger, J.T., Bloomfield, D.M., & Steinman, R.C. (1997). Physical fitness as a determinant of vagal modulation. Medicine and Science in Sports and Exercise, 29, 812-817.

Goldsmith, R.L., Bigger, J.T., Steinman, R.C., & Fleiss, J.L. (1992). Comparison of 24-hour parasympathetic activity in endurance-trained and untrained young men. Journal of the American College of Cardiology, 20, 552-558.

Goldstein, D.S., Lake, C.R., Chernow, B., Ziegler, M.G., Coleman, M.D., Taylor, A.A., Mitchell, J.R., Kopin, I.J., & Keiser, H.R. (1983). Age-dependence of hypertesive-normotensive differences in plasma norepinephrine. Hypertension Dallas, 5, 100-104.
Gorman, A.J., & Proppe, D.W. (1984). Mechanisms producing tachycardia in conscious baboons during environmental heat stress. Journal of Applied Physiology, 56, 441-446.

Grassi, G., Bolla, G.B., Turri, C., Bertinieri, G., Pozzi, M., & Mancia, G. (1996). Old and new approaches for evaluating autonomic control of circulation in man. Contributions to Nephrology, 119, 165-172.

Grassi, G., Seravalle, G., Calhoun, D.A., & Mancia, G. (1994). Physical training and baroreceptor control of sympathetic nerve activity in humans. Hypertension, 23, 294-301.

Gregoire, J., Tuck, S., Yamamoto, Y., & Hughson, R.L. (1996). Heart rate variability at rest and exercise: influence of age, gender, and physical training. Canadian Journal of Applied Physiology, 21, 455-470.

Greiwe, J.S., Hickner, R.C., Shah, S.D., Cryer, P.E., & Holloszy, J.O. (1999). Norepinephrine response to exercise at the same relative intensity before and after endurance exercise training. Journal of Applied Physiology, 86, 531-535.

Gross, P.M., Whipp, B.J., Davidson, J.T., Koyal, S.N., & Wasserman, K. (1976). Role of the carotid bodies in the heart rate response to breath holding in man. Journal of Applied Physiology, 41, 336-340.

Gutin, B., Owens, S., Slavens, G., Riggs, S., & Treiber, F. (1997). Effect of physical training on heart-period variability in obese children. Journal of Pediatrics, 130, 938-943.

Gutrecht, J.A. (1994). Sympathetic skin response. Journal of Clinical Neurophysiology, 11, 519-524.

Guyton, A.C., & Hall, J.E. (1994). Textbook of Medical Physiology (9th ed.). Philadelphia: W.B. Saunders Company.

Hagberg, J.M., Goldring, D., Heath, G.W., Ehsani, A.A., Hernandez, A., & Holloszy, J.O. (1984). Effects of exercise-training on plasma catecholamines and haemodynamics of adolescent hypertensives during rest, submaximal exercise, and orthostatic stress. Clinical Physiology, 4, 117-124.

Hagberg, J.M., Seals, D.R., Yerg, J.E., Gavin, J., Gingerich, R., Premachandra, B., & Holloszy, J.O. (1988). Metabolic responses to exercise in young and older athletes and sedentary men. Journal of Applied Physiology, 65, 900-908.

Hainsworth, R., Karim, F., & Sofola, O.A. (1979). Left ventricular inotropic responses to stimulation of carotid body chemoreceptors in anaesthetised dogs. Journal of Physiology, 287, 455-466.

Hallin, R.G., & Torebjork, H.E. (1974). Single unit activity in human skin nerves during rest and various manoeuvres. Acta Physiologica Scandinavica, 92, 303-317.
Hartley, L.H., Mason, J.W., Hogan, R.P., Jones, L.G., Kotchen, T., Mougey, E.H., Wherry, F.E., Pennington, L.L., & Ricketts, P.T. (1972a). Multiple hormonal responses to graded exercise in relation to physical training. Journal of Applied Physiology, 33, 602-606.

Hartley, L.H., Mason, J.W., Hogan, R.P., Jones, L.G., Kotchen, T., Mougey, E.H., Wherry, F.E., Pennington, L.L., & Ricketts, P.T. (1972b). Multiple hormonal responses to prolonged exercise in relation to physical training. Journal of Applied Physiology, 33, 607-610.

Hayano, J., Sakakibara, Y., Yamada, A., Yamada, M., Mukai, S., Fujinami, T., Yokoyama, K., Watanabe, Y., & Takata, K. (1991). Accuracy of assessment of cardiac vagal tone by heart rate variability in normal subjects. American Journal of Cardiology, 67, 199-204.

Hayashi, N., Nakamura, Y., & Muraoka, I. (1992). Cardiac autonomic regulation after moderate and exhaustive exercise. Annals of Physiological Anthropology, 11, 333-338.

He, J., Klag, M.J., Appel, L.J., Charleston, J., & Whelton, P.K. (1999). The renin-angiotensin system and blood pressure: differences between blacks and whites. American Journal of Hypertension, 12, 555-562.

Hirsch, J.A., & Bishop, B. (1981). Respiratory sinus arrhythmia in humans – how breathing patterns modulate heart rate. American Journal of Physiology, 241, H620-H629.

Hjemdahl, P. (1984). Inter-laboratory comparison of plasma catecholamine determinations using several different assays. Acta Physiologica Scandinavica, 527 (Suppl.), 43-54.

Hoeldtke, R.D., Davis, K.M., Hshich, P.B., Gaspar, S.R., & Dworkin, G.E. (1992). Autonomic surface potential analysis: assessment of reproducibility and sensitivity. Muscle and Nerve, 15, 926-931.

Hohimer, A.R., Hales, J.R., Rowell, L.B., & Smith, O.A. (1983). Regional distribution of blood flow during mild dynamic leg exercise in the baboon. Journal of Applied Physiology, 55, 1173-1177.

Hohnloser, S.H., Klingenheben, T., Zabel, M., Schroder, F., & Just, H. (1992). Intraindividual reproducibility of heart rate variability. Pacing and Clinical Electrophysiology, 15, 2211-2214.

Hollander, A.P., & Bouman, L.N. (1975). Cardiac acceleration in man elicited by a muscle-heart reflex. Journal of Applied Physiology, 38, 272-278.

Hollander, A., & Seraganian, P. (1984). Aerobic fitness and psychophysiological reactivity. Canadian Journal of Behavioral Science, 16, 257-261.

Holloszy, J.O., & Both, F.W. (1976). Biochemical adaptations to endurance exercise training. Annual Review of Physiology, 38, 273-291.

Holmes, D.S., & McGilley, B.M. (1987). Influence of a brief aerobic training program on heart rate and subjective response to a psychological stressor. Psychosomatic Medicine, 49, 366-374.

Holmes, D.S., & Roth, D.L. (1985). Association of aerobic fitness with pulse rate and subjective responses to psychological stress. Psychophysiology, 22, 525-529.

Honda, Y., Hashizume, I., Kimura, H., & Severinghaus, J.W. (1988). Bilateral carotis body resection in man enhances hypoxic tachycardia. Japanese Journal of Physiology, 38, 917-928.

Horodyski, M.B., De Meersman, R.E., Vandenburgh, P.M., & Gallagher, D. (1995). With environmental control, the effects of race and sex on blood pressure regulatory mechanisms appear diminished. Journal of Human Hypertension, 9, 107-111.

Howorka, K., Pumpria, J., Haber, P., Koller-Strametz, J., Mondrzyk, J., & Schabmann, A. (1997). Effects of physical training on heart rate variability in diabetic patients with various degrees of cardiovascular autonomic neuropathy. Cardiovascular Research, 34, 206-214.

Hudson, D.L., Smith, M.L., & Raven, P.B. (1987). Physical fitness and hemodynamic response of women to lower body negative pressure. Medicine and Science in Sports and Exercise, 19, 375-381.

Hughson, R.L., Yamamoto, Y., McCullough, R.E., Sutton, J.R., & Reeves, J.T. (1994). Sympathetic and parasympathetic indicators of heart rate control at altitude studied by spectral analysis. Journal of Applied Physiology, 77, 2537-2542.

Huikuri, H.V., Kessler, K.M., Terracall, E., Castellanos, A, Linnaluoto, M.K., & Myerburg, R.J. (1990). Reproducibility and circadian rhythm of heart rate variability in healthy subjects. American Journal of Cardiology, 65, 391-393.

Huikuri, H.V., Pikkujamsa, S.M., Airaksinen, J., Ikaheimo, M.J., Raotala, A.O., Kauma, H., Lilja, M., & Kesaniemi, A. (1996). Sex-related differences in autonomic modulation of heart rate in middle-aged subjects. Circulation, 94, 122-125.

Hull, E.M., Young, S.H., & Ziegler, M.G. (1984). Aerobic fitness affects cardiovascular and catecholamine responses to stressors. Psychophysiology, 21, 353-360.

Hypertension Detection and Follow-up Program Cooperative Group. (1979). Five year findings of the hypertension detection and follow-up program, II: mortality by race, sex, and age. Journal of the American Medical Association, 242, 2572-2577.

Iellamo, F., Legramante, J.M., Raimondi, G., & Peruzzi, G. (1997). Baroreflex control of sinus node during dynamic exercise in humans: effects of central command and muscle reflexes. American Journal of Physiology, 272, H1157-H1164.

Iellamo, F., Legramante, J.M., Raimondi, G., Castrucci, F., Massaro, M., & Peruzzi, G. (1996). Evaluation of reproducibility of spontaneous baroreflex sensitivity at rest and during laboratory tests. Journal of Hypertension, 14, 1099-1104.

Iida, R., Hirayanagi, K., Iwasaki, K., Ogawa, S., Suzuki, H., & Yajima, K. (1999). non-invasive assessment of human baroreflex during different body positions. Journal of the Autonomic Nervous System, 75, 164-170.

Jain, S.K., Subramanian, S., Julka, D.B., & Guz, A. (1972). Search for evidence of lung chemo-reflexes in man: study of respiratory and circulatory effect of phenyl dignanide and lobeline. Clinical Science, 42, 163-177.

James, G., Pickering, T.G., Yee, L.S., Harshfield, G.A., Riva, S., & Laragh, J.G. (1988). The reproducibility of average ambulatory, home, and clinic pressures. Hypertension, 11, 545-549.

Janssen, M.J.A., de Bie, J., Swenne, C.A., & Oudhof, J. (1993). Supine and standing sympathovagal balance in athletes and controls. European Journal of Applied Physiology, 67, 164-167.

Jennings, G., Nelson, L., Nestel, P., Esler, M., Korner, P., Burton, D., & Bazelmans, J. (1986). The effects of changes in physical activity on major cardiovascular risk factors, hemodynamics, sympathetic function, and glucose utilization in man: a controlled study of four levels of activity. Circulation, 73, 30-40.

Johns, D.R., Gress, D.R., Shahani, B.T., & Young, R.R. (1986). Electrophysiologic evaluation of autonomic function in Parkinson's disease. Muscle and Nerve (Abstract), 9, 657.

Jost, J., Weiss, M., & Weicker, H. (1989). Comparison of sympathoadrenergic regulation at rest, and of the adrenoreceptor system in swimmers, long distance runners, weight lifters, wrestlers, and untrained men. European Journal of Applied Physiology, 58, 591-604.

Jost, J., Weiss, M., & Weicker, H. (1990). Sympathoadrenergic regulation and the adrenoreceptor system. Journal of Applied Physiology, 68, 897-904.

Kamath, M.V., & Fallen, E.L. (1993). Power spectral analysis of heart rate variability: a noninvasive signature of cardiac autonomic function. Critical Reviews in Biomedical Engineering, 21, 245-311.

Kamath, M.V., Fallen, E.L., & McElvie, R. (1991). Effects of steady state exercise on the power spectrum of heart rate variability. Medicine and Science in Sports and Exercise, 23, 428-434.

Katona, P.G., McLean, M., Dighton, D.H., & Guz, A. (1982). Sympathetic and parasympathetic cardiac control in athletes and nonathletes at rest. Journal of Applied Physiology, 52, 1652-1657.

Keller, S., & Seraganian, P. (1984). Physical fitness level and autonomic reactivity in psychosocial stress. Journal of Psychosomatic Research, 28, 279-287.

Kenney, W.L. (1985). Parasympathetic control of resting heart rate: relationship to aerobic power. Medicine and Science in Sports and Exercise, 17, 451-455.

Ketelhut, R.G., Franz, I.W., & Scholze, J. (1997). Efficacy and position of endurance training as a non-drug therapy in the treatment of arterial hypertension. Journal of Human Hypertension, 11, 651-655.

Kiilavuori, K., Toivonen, L., Naveri, H., & Leinonen, H. (1995). Reversal of autonomic derangements by physical training in chronic heart failure assessed by heart rate variability. European Heart Journal, 16, 490-495.

Kingwell, B.A., Dart, A.M., Jennings, G.L., & Korner, P.I. (1992). Exercise training reduces the sympathetic component of the blood pressure-heart rate baroreflex in man. Clinical Science, 82, 357-362.

Kinugasa, H., & Hirayanagi, K. (1999). Effects of skin surface cooling and heating on autonomic nervous activity and baroreflex sensitivity in humans. Experimental Physiology, 84, 369-377.

Kiyonaga, A., Arakawa, K., Tanaka, H., & Shindo, H. (1985). Blood pressure and hormonal responses to aerobic exercise. Hypertension, 7, 125-131.

Kjaer, M., Christensen, N.J., Sonne, B., Richter, E.A., & Galbo, H. (1985). Effect of exercise on epinephrine turnover in trained and untrained male subjects. Journal of Applied Physiology, 59, 1061-1067.

Kjaer, M., Mikines, K.J., Christensen, N.J., Tronier, B., Vinten, J., Sonne, B., Richter, E.A., & Galbo, H. (1984). Glucose turnover and hormonal changes during insulin-induced hypoglycemia in trained humans. Journal of Applied Physiology, 57, 21-27.

Kleiger, R.E., Bigger, J.T., Bosner, M.S., Chung, M.K., Cook, J.R., Rolnitzky, L.M., Steinman, R., & Fleiss, J.L. (1991). Stability over time of variables measuring heart rate variability in normal subjects. American Journal of Cardiology, 68, 626-630.

Koller, E.A., Drechsel, S., Hess, T., Macherel, P., & Boutellier, U. (1988). Effects of atropine and propranolol on the respiratory, circulatory, and ECG responses to high altitude in man. European Journal of Applied Physiology, 57, 163-172.

Kopin, I.J., Hertting, G., & Gordon, E.K. (1962). Fate of norepinephrine-H3 in the isolated perfused rat heart. Journal of Pharmacologic and Experimental Therapy, 138, 34.

Krasney, J.A., Levitzky, M.G., & Koehler, R.C. (1974). Sinoaortic contribution to the adjustment of systemic resistance in exercising dogs. Journal of Applied Physiology, 36, 679-685.

Krogh, A., & Lindhard, J. (1913). The regulation of respiration and circulation during the initial stages of muscular work. Journal of Physiology, 47, 112-136.

Kuramoto, K., Matsushita, S., Mifune, J., Sakai, M., & Murakami, M. (1978). Electrocardiographic and hemodynamic evaluations of isoproterenol test in elderly ischemic heart disease. Japanese Circulation Journal, 42, 955-960.

Laitinen, T., Hartikainen, J., Vanninen, E., Niskanen, L., Geelen, G., & Lansimies, E. (1998). Age and gender dependency of baroreflex sensitivity in healthy subjects. Journal of Applied Physiology, 84, 576-583.

Lakatta, E.G. (1993). Cardiovascular regulatory mechanisms in advanced age. Physiological Reviews, 73, 413-467.

Lake, B.W., Suarez, E.C., Schneiderman, N., & Tocci, N. (1985). The type A behavior pattern, physical fitness, and psychophysiological reactivity. Health Psychology, 4, 169-187.

La Rovere, M.T., Mortara, A., Sandrone, G., & Lombardi, F. (1992). Autonomic nervous system adaptations to short-term exercise training. Chest, 101 (Suppl. 5), 299S-303S.

LeBlanc, J., Nadeau, A., Richard, D., & Tremblay, A. (1982). Variations in plasma glucose, insulin, growth hormone and catecholamines in response to insulin in trained and non-trained subjects. Metabolism, 5, 453-456.

LeBlanc, P.R., & Rakusan, K. (1987). Effects of age and isoproterenol on the cardiac output and regional blood flow in the rat. Canadian Journal of Cardiology, 3, 246-250.

Lehmann, M., Dickhuth, H., Schmid, P., Porzig, H., & Keul, J. (1984). Plasma catecholamines, beta adrenergic receptors, and isoproterenol sensitivity in endurance trained and non-endurance trained volunteers. European Journal of Applied Physiology, 52, 362-369.

Lehmann, M., & Keul, J. (1986). Free plasma catecholamines, heart rates, lactate levels, and oxygen uptake in competition weight lifters, cyclists, and untrained control subjects. International Journal of Sports Medicine, 7, 18-21.

Lehmann, M., Schmid, P., & Keul, J. (1984). Age- and exercise-related sympathetic activity in untrained volunteers, trained athletes and patients with impaired left-ventricular contractility. European heart Journal, 5 (Suppl. E), 1-7.

Leimbach, W. N., Wallin, G. B., Victor, R. G., Aylward, P. E., Sundlof, G., & Mark, A. L. (1986). Direct evidence from intraneural recordings for increased sympathetic outflow in patients with heart failure. Circulation, 78, 913-919.

Leitch, J.A., Newling, R.P., Basta, M., Inder, K., Dear, K., & Fletcher, P.J. (1997). Randomized trial of a hospital-based exercise training program after acute myocardial infarction: cardiac autonomic effects. Journal of the American College of Cardiology, 29, 1263-1268.

Levine, B.D., Buckey, J.C., Fritsch, J.M., Yancy, C.W., Watenpaugh, D.E., Snell, P.G., Lane, L.D., Eckberg, D.L., & Blomqvist, C.G. (1991). Physical fitness and cardiovascular regulation: mechanisms of orthostatic intolerance. Journal of Applied Physiology, 70, 112-122.

Levy, M.N. (1984). Cardiac sympathetic-parasympathetic interactions. Federation Proceedings, 43, 2598.

Levy, W.C., Cerqueira, M.D., Harp, G.D., Johannessen, K., Abrass, I.B., Schwartz, R.S., & Stratton, J.R. (1998). Effect of endurance exercise training on heart rate variability at rest in healthy young and older men. American Journal of Cardiology, 82, 1236-1241.

Liao, D., Barnes, R.W., Chambless, L.E., Simpson, R.J., Sorlie, P., & Heiss, G. (1995). Age, race, and sex differences in autonomic cardiac function measured by spectral analysis of heart rate variability – The ARIC study. American Journal of Cardiology, 76, 906-912.

Light, K.C., Obrist, P.A., James, S.A., & Strogatz, D.S. (1987). Cardiovascular responses to stress: II. Relationships to aerobic exercise patterns. Psychophysiology, 24, 79-86.

Lightfoot, J.T., Claytor, R.P., Torok, D.J., Journell, T.W., & Fortney, S.M. (1989). Ten weeks of aerobic training do not affect lower body negative pressure responses. Journal of Applied Physiology, 67, 894-901.

Loffelholz, K., & Pappano, A.J. (1985). The parasympathetic neuroeffector junction of the heart. Pharmacological Reviews, 37, 1.

London, G.M., Safar, M.E., Weiss, Y.A., & Milliez, P.L. (1976). Isoproterenol sensitivity and total body clearance of propranolol in hypertensive patients. Journal of Clinical Pharmacology, 16, 174-183.

Ludbrook, J., & Graham, W.F. (1985). Circulatory responses to onset of exercise: role of arterial and cardiac baroreflexes. American Journal of Physiology, 248, H457-H467.

Luft, V.C, Myrhe, L.G., Leoppky, J.A., & Venters, M.D. (1976). A study of factors affecting tolerance of gravitational stress simulated by lower body negative pressure. Albuquerque, NM: Lovelace Foundation.

Maciel, B.C., Gallo, L., Marin Neto, J.A., Lima Filho, E.C., & Martins, L.E. (1986). Autonomic nervous control of the heart rate during dynamic exercise in normal man. Clinical Science, 71, 457-460.

Maciel, B.C., Gallo, L., Marin Neto, J.A., Lima Filho, E.C., Terra Filho, J., & Manco, J.C. (1985). Parasympathetic contribution to bradycardia induced by endurance training in man. Cardiovascular Research, 19, 642-648.

Mack, G.W., Nose, H., & Nadel, E.R. (1988). Role of the cardiopulmonary baroreflexes during dynamic exercise. Journal of Applied Physiology, 65, 1827-1832.

Mack, G.W., Shi, X.G., Nose, H., Tripathi, A., & Nadel, E.R. (1987). Diminished baroreflex control of forearm vascular resistance in physically fit humans. Journal of Applied Physiology, 63, 105-110.

Malfatto, G., Facchini, M., Bragato, R., Branzi, G., Saia, L., & Leonetti, G. (1996). Short and long term effects of exercise training on the tonic autonomic modulation of heart rate variability after myocardial infarction. European Heart Journal, 17, 532-538.

Malik, M. (1998). Heart rate variability. Current Opinion in Cardiology, 13, 36-44.

Malliani, A., Pagani, M., Lombardi, F., & Ceruti, S. (1991). Cardiovascular neural regulation explored in the frequency domain. Circulation, 84, 482-492.

Malliani, A. (1986). Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog. Circulation Research, 59, 178-193.

Mancia, G., & Grassi, G. (1991). Assessment of sympathetic cardiovascular influences in man: haemodynamic and humoral markers versus microneurography. Clinical Autonomic Research, 1, 245-249.

Marks, B.L., & Lightfoot, J.T. (1999). Reproducibility of resting heart rate variability with short sampling periods. Canadian Journal of Applied Physiology, 24, 337-348.

Marshall, J.M. (1994). Peripheral chemoreceptors and cardiovascular regulation. Physiological Reviews, 74, 543-594.

Matsukawa, T., Sugiyama, Y., Watanabe, T., Kobayashi, F., & Mano, T. (1999). Gender differences in age-related changes in muscle sympathetic nerve activity in healthy subjects. American Journal of Physiology, 275, R1600-R1604.

Mazzeo, R.S., Bender, P.R., Brooks, G.A., Butterfield, G.E., Groves, B.M., Sutton, J.R., Wolfel, E.E., & Reeves, J.T. (1991). Arterial catecholamine responses during exercise with acute and chronic high-altitude exposure. American Journal of Physiology, 261, E419-E424.

Mazzeo, R.S., Wolfel, E.E., Butterfield, G.E., & Reeves, J.T. (1994). Sympathetic response during 21 days at high altitude (4300 m) as determined by urinary and arterial catecholamines. Metabolism, 43, 1226-1232.

McCrimmon, D.R., Cunningham, D.A., Rechnitzer, P.A., & Griffiths, J. (1976). Effect of training on plasma catecholamines in post myocardial infarction patients. Medicine and Science in Sports and Exercise, 8, 152-156.

McCubbin, J.A., Cheung, R., Montgomery, T.B., Bulbulian, R., & Wilson, J.F. (1992). Aerobic fitness and opioidergic inhibition of cardiovascular stress reactivity. Psychophysiology, 29, 687-697.

Melcher, A., & Donald, D.E. (1981). Maintained ability of carotid baroreflex to regulate arterial pressure during exercise. American Journal of Physiology, 241, H838-H849.

Metelka, R., Weinbergova, O., Opavsky, J., Salinger, J., & Ostransky, J. (1999). Short-term heart rate variability changes after exercise training in subjects following myocardial infarction. Acta Universitatis Palackianae Olomucensis Facultatis Medicae, 142, 79-82.

Mitchell, J.H. (1990). Neural control of the circulation during exercise. Medicine and Science in Sports and Exercise, 22, 141-154.

Mitchell, J.H., & Schmidt, R.F. (1983). Cardiovascular reflex control by afferent fibres from skeletal muscle receptors. In Handbook of Physiology. The Cardiovascular System, Peripheral Circulation and Organ Blood Flow, vol. 3 (ed. J.T. Shephard, F.M. Abboud and S.R. Geiger), pp. 623-658. Bethesda: American Physiological Society.

Montagna, P., Salvi, F., & Liguori, R. (1988). sympathetic skin response in familial amyloid polyneuropathy. Muscle and Nerve, 11, 183-184.

Myrtek, M., & Foerster, F. (1986). The Law of Initial Value: a rare exception. Biological Psychology, 22, 227-237.

Nakamura, Y., Yamamoto, Y., & Murskoa, I. (1993). Autonomic control of the heart rate during physical exercise and fractal dimension of heart rate variability. Journal of Applied Physiology, 74, 875-881.

Ng, A.V., Callister, R., Johnson, D.G., & Seals, D.R. (1993). Age and gender influence of muscle sympathetic nerve activity at rest in healthy humans. Hypertension Dallas, 21, 498-503.

Ng, A.V., Callister, R., Johnson, D.G., & Seals, D.R. (1994). Endurance exercise training is associated with elevated basal sympathetic nerve activity in healthy older humans. Journal of Applied Physiology, 77, 1366-1374.

Niimi, Y., Matsukawa, T., Sugiyama, Y., Shamsuzzaman, A.S., Ito, H., Sobue, G., & Mano, T. (1997). Effect of heat stress on muscle sympathetic nerve activity in humans. Journal of the Autonomic Nervous System, 63, 61-67.

Nolan, J., Flapan, A.D., Capewell, S., MacDonald, T.M., Neilson, J.M., & Ewing, D.J. (1992). Decreased cardiac parasympathetic activity in chronic heart failure and its relation to left ventricular function. British Heart Journal, 67, 482-485.

Nolan, J., Flapan, A.D., Goodfield, N.E., Prescott, R.J., Bloomfield, P., Neilson, J.M.M., & Ewing, D.J. (1996). Measurement of parasympathetic activity from 24-hour ambulatory electrocardiograms and its reproducibility and sensitivity in normal subjects, patients with symptomatic myocardial ischemia, and patients with diabetes mellitus. American Journal of Cardiology, 77, 154-158.

Nye, P.C.G. (1994). Identification of peripheral chemoreceptor stimuli. Medicine and Science in Sports and Exercise, 26, 311-318.

Oberg, B. (1964). Effects of cardiovascular reflexes on net capillary fluid transfer. Acta Physiologica Scandinavica, 62 (Suppl. 229), 1-98.

Oberg, B., & White, S. (1970). Circulatory effects of interruption and stimulation of cardiac vagal afferents. Acta Physiologica Scandinavica, 80, 383-94.

O'Conner, S.W., Scarpace, P.J., & Abrass, I.B. (1981). Age-associated decrease of adenylate cyclase activity in rat myocardium. Mechanisms of Ageing and Development, 16, 91-95.

O'Leary, D.S. (1993). Autonomic mechanisms of muscle metaboreflex control of heart rate. Journal of Applied Physiology, 74, 1748-1754.

O'Leary, D.S., Rossi, N.F., & Churchill, P.C. (1993). Muscle metaboreflex control of vasopressin and renin release. American Journal of Physiology, 264, H1422-H1427.

Oleshansky, M.A., Zoltick, J.M., Herman, R.H., Mougey, E.H., & Meyerhoff, J.L. (1990). The influence of fitness on neuroendocrine responses to exhaustive treadmill exercise. European Journal of Applied Physiology, 59, 405-410.

O'Mahony, D., Bennett, C., Green, A., & Sinclair, A.J. (2000). Reduced baroreflex sensitivity in elderly humans is not due to efferent autonomic dysfunction. Clinical Science, 98, 103-110.

Oya, M., Itoh, H., Kato, K., Tanabe, K., & Murayama, M. (1999). Effects of exercise training on the recovery of the autonomic nervous system and exercise capacity after acute myocardial infarction. Japanese Circulation Journal, 63, 843-848.

Pace, N., Grinswold, R.L., & Grunbaum, B.W. (1964). Increase in urinary norepinephrine excretion during 14 days sojourn at 3800 meters elevation. Federation Proceedings, 23, 521.
Pagani, M., Lombardi, F., Guzzetti, S., Rimoldi, O., Furlan, R., Pizzinelli, P., Sandrone, G., Malfatto, G., Dell'Orto, S., Piccaluga, E., Turiel, M., Baselli, G., Cerutti, S., &

Pagani, M., Somers, V., Furlan, R., Dell'Orto, S., Conway, J., Baselli, G., Cerutti, S., Sleight, P., & Malliani, A. (1988). Changes in autonomic regulation induced by physical training in mild hypertension. Hypertension, 12, 600-610.

Paintal, A.S. (1973). Vagal sensory receptors and their reflex effects. Physiological Reviews, 53, 159-227.

Pan, H.Y., Hoffman, B.B., Pershe, R.A., & Blaschke, T.F. (1986). Decline in beta-adrenergic receptor-mediated vascular relaxation with aging in man. Journal of Pharmacology and Experimental Therapeutics, 239, 802-807.

Papelier, Y., Escourrou, P., Gauthier, J.P., & Rowell, L.B. (1994). Carotid baroreflex control of blood pressure and heart rate in men during dynamic exercise. Journal of Applied Physiology, 77, 502-506.

Parati, G., Saul, J.P, Di Rienzo, M., & Mancia, G. (1995). Spectral analysis of heart rate and blood pressure variability in evaluating cardiovascular regulation: A critical appraisal. Hypertension, 25, 1276-1286.

Parati, G., Pomidossi, G., Casadei, R., Ravogli, A., Groppelli, A., Cesana, B., & Mancia, G. (1988). Comparison of the cardiovascular effects of different laboratory stressors and their relationship with blood pressure variability. Journal of Hypertension, 6, 481-488.

Parati, G., Pomidossi, G., Ramirez, A., Cesana, B., & Mancia, G. (1985). Variability of the haemodynamic responses to laboratory tests employed in assessment of neural cardiovascular regulation in man. Clinical Science, 69, 533-540.

Parsons, S., Scott, A.R., & Macdonald, I.A. (1992). The effect of posture and environmental temperature on cardiovascular reflexes in normal subjects and diabetes mellitus. Clinical Autonomic Research, 2, 147-151.

Paynter, D.E., Tipton, C.M., & Tcheng, T. (1977). Response of immunosympathectomized rats to training. Journal of Applied Physiology, 42, 935-940.

Perini, R., Milesi, S., Biancardi, L., Pendergast, D.R., & Veicsteinas, A. (1998). Heart rate variability in exercising humans: effect of water immersion. European Journal of Applied Physiology, 77, 326-332.

Perini, R., Orizio, C., Baselli, G., Cerutti, S., & Veicsteinas, A. (1990). The influence of exercise intensity on the power spectrum of heart rate variability. European Journal of Applied Physiology, 61, 143-148.

Perini, R., Orizio, C., Milesi, S., Biancardi, L., Baselli, G., & Veicsteinas, A. (1993). Body position effects the power spectrum of heart rate variability during dynamic exercise. European Journal of Applied Physiology, 66, 207-213.

Perkins, K.A., Dubbert, P.M., Martin, J.E., Faulstich, M.E., & Harris, J.K. (1986). Cardiovascular reactivity to psychological stress in aerobically trained versus untrained mild hypertensives and normotensives. Health Psychology, 5, 407-421.

Peronnet, F., Cleroux, J., Perrault, H., Cousineau, D., De Champlain, J., & Nadeau, R. (1981). Plasma norepinephrine response to exercise before and after training in humans. Journal of Applied Physiology, 51, 812-815.

Pfeifer, M., Cook, D., Brodsky, J., Tice, D., Parrish, D., Reenan, A., Halter, J.B., & Porte, D. Jr. (1982). Quantitative evaluation of cardiac parasympathetic neuropathy in normal and diabetic men. Diabetes, 31, 339-345.

Pfeifer, M.A., Weinberg, C.R., Cook, D., Best, J.D., Reenan, A., & Halter, J.B. (1983). Differential changes of autonomic nervous system function with age in man. American Journal of Medicine, 75, 249-258.

Pieper, S.J., & Hammill, S.C. (1995). Heart rate variability: technique and investigational aplications in cardiovascular medicine. Mayo Clinic Proceedings, 70, 955-964.

Piepoli, M., Radaelli, A., Ponikowski, P., Adamopoulos, S., Bernardi, L., Sleight, P., & Coats, A.J.S. (1996). Reproducibility of heart rate variability indices during exercise stress testing and inotrope infusion in chronic heart failure patients. Clinical Science, 91 (Suppl.), 87-88.

Pitzalis, M.V., Mastropasqua, F., Massari, F., Forleo, C., DiMaggio, M., Passantino, A., Colombo, R., DiBiase, M., & Rizzon, P. (1996). Short- and long-term reproducibility of time and frequency domain heart rate variability measurements in normal subjects. Cardiovascular Research, 32, 226-233.

Plante, T.G., & Karpowitz, D. (1987). The influence of aerobic exercise on physiologic stress reactivity. Psychophysiology, 24, 670-677.

Poehlman, E.T., McAuliffe, T., & Danforth, E. (1990). Effects of age and level of physical activity on plasma norepinephrine kinetics. American Journal of Physiology, 258, E256-E262.

Pomeranz, B., Macaulay, R.J.B., Caudill, M.A., Kutz, I., Adam, D., Gordon, D., Kilborn, K.M., Barger, A.C., Shannon, D.C., & Cohen, R.J. (1985). Assessment of autonomic function in man by heart rate analysis. American Journal of Physiology, 248, H151-H153.

Ponchia, A., Noventa, D., Bertaglia, M., Carretta, R., Zaccaria, M., Miraglia, G., Pascotto, P., & Buja, G. (1994). Cardiovascular neural regulation during and after prolonged high altitude exposure. European Heart Journal, 15, 1463-1469.

Potts, J.T., Shi, X.R., & Raven, P.B. (1995). Cardiopulmonary baroreceptors modulate carotid baroreflex control of heart rate during dynamic exercise in humans. American Journal of Physiology, 268, H1567-H1576.

Potts, J.T., Shi, X.R., & Raven, P.B. (1993). Carotid baroreflex responsiveness during dynamic exercise in humans. American Journal of Physiology, 265, H1928-H1938.

Prabhakar N.R., Landis, S.C., Kumar, G.K., Mullikin-Kilpatrick, D., Cherniak, N.S., & Leeman, S. (1989). Substance P and neurokinin A in the cat carotid body: localization, exogenous effects and changes in content in response to arterial pO_2. Brain Research, 481, 205-214.

Prinz, P.N., Halter, J., Benedetti, C., & Raskind, M. (1979). Circadian variation of plasma catecholamines in young and old men. Journal of Clinical Endocrinology and Metabolism, 49, 300-304.

Radaelli, A., Coats, A.J.S., Leuzzi, S., Piepoli, M., Meyer, T.E., Calciati, A., Finardi, G., Bernardi, L., & Sleight, P. (1996). Physical training enhances sympathetic and parasympathetic control of heart rate and peripheral vessels in chronic heart failure. Clinical Science, 91, 92-94.

Raszewa, M., Hausmanowa-Petrusewicz, I., Blaszczyk, M., & Jablonska, S. (1991). Sympathetic skin response in scleroderma. Electromyography and Clinical Neurophysiology, 31, 467-472.

Raven, P.B., Potts, J.T., & Shi, X. (1997). Baroreflex regulation of blood pressure during dynamic exercise. Exercise and Sport Sciences Reviews, 25, 365-390.

Raven, P.B., Rohm-Young, D., & Blomqvist, C.G. (1984). Physical fitness and cardiovascular response to lower body negative pressure. Journal of Applied Physiology, 56, 138-144.

Ray, C.A., & Hume, K.M. (1998). Sympathetic neural adaptations to exercise training in humans: insights from microneurography. Medicine and Science in Sports and Exercise, 30, 387-391.

Ray, C.A., Pace, W.M., & Clary, M.P. (1992). Sympathetic and cardiovascular adaptations to dynamic one-legged exercise training (Abstract). The Physiologist, 34, 235.

Reilling, M.J., & Seals, D.R. (1988). Respiratory sinus arrhythmia and carotid baroreflex control of heart rate in endurance athletes and untrained controls. Clinical Physiology, 8, 511-519.

Robbe, H.W.J., Mulder, L.J.M., Ruddel, H., Langewitz, W.A., Veldman, J.B.P., & Mulder, G. (1987). Assessment of baroreflex sensitivity by means of spectral analysis. Hypertension, 10, 538-543.

Robinson, B.F., Epstein, S.E., Beiser, G.D., & Braunwald E. (1966). Control of heart rate by the autonomic nervous system. Circulation Research, 19, 400-411.

Rogers, M.W., Probst, M.M., Gruber, J.J., Berger, R., & Boone, J.B. (1996). Differential effects of exercise training intensity on blood pressure and cardiovascular responses to stress in borderline hypertensive humans. Journal of Hypertension, 14, 1369-1375.

Rosenblueth, A., & Simeone, F.A. (1936). The interrelations of vagal and accelerator effects on the cardiac rate. American Journal of Physiology, 110, 42-55.

Roskies, E., Seraganian, P., Oseasohn, R., Hanley, J.A., Collu, R., Martin, N., & Smilga, C. (1986). The Montreal Type A Intervention Project: major findings. Health Psychology, 5, 45-69.

Rossy, L.A., & Thayer, J.F. (1998). Fitness and gender-related differences in heart period variability. Psychosomatic Medicine, 60, 773-781.

Rothman, J. L. S., Easty, A. C., Frecker, R. C., & Floras, J. S. (1991). Development and evaluation of two automated methods for quantifying human muscle sympathetic nerve activity. Computers in Biology and Medicine, 21, 221-235.

Rowe, J.W., & Troen, B.R. (1980). Sympathetic nervous system and aging in man. Endocrine Reviews, 1, 167-179.

Rowell, L.B. (1986). Human Circulation: Regulation During Physical Stress. New York: Oxford Press.

Rowell, L.B. (1993). Human Cardiovascular Control. New York: Oxford Press.

Rowell, L.B., Hermansen, L., & Blackmon, J.R. (1976). Human cardiovascular and respiratory responses to graded muscle ischemia. Journal of Applied Physiology, 41, 693-701.

Rubin, P.C., Scott, P.J., McLean, K., & Reid, J.L. (1982). Noradrenaline release and clearance in relation to age and blood pressure in man. European Journal of Clinical Investigation, 12, 121-125.

Ryan, S.M., Goldberger, A.L., Pincus, S.M., Mietus, J., & Lipsitz, L.A. (1994). Gender- and age-related differences in heart rate dynamics: Are women more complex than men? Journal of the American College of Cardiology, 24, 1700-1707.

Sacknoff, D.M., Gleim, G.W., Stachenfeld, N., & Coplan, N.L. (1994). Effect of athletic training on heart rate variability. American Heart Journal, 127, 1275-1278.

Saito, M., Watanabe, H., & Mano, T. (1993). Comparison of muscle sympathetic nerve activity during exercise in dominant and nondominant forearm. European Journal of Applied Physiology, 66, 108-115.

Saltin, B., & Astrand, P.O. (1967). Maximal oxygen uptake in athletes. Journal of Applied Physiology, 23, 353-358.

Sanders, J.S., Ferguson, D.W., & Mark, A.L. (1988). Arterial baroreflex control of sympathetic nerve activity during elevation of blood pressure in normal man: dominance of aortic baroreflexes. Circulation, 77, 279-288.

Saul, J.P. (1990). Beat-to-beat variations of heart rate reflect modulation of cardiac autonomic outflow. News in Physiological Sciences, 5, 32-37.

Savard, G.K., & Lundie, M.J. (1994). Carotid-cardiac baroreflex and training status: significance of initial responsiveness. Canadian Journal of Physiology and Pharmacology, 73, 98-106.

Schachter, J., & Kuller, L.H. (1984). Blood volume expansion among blacks: an hypothesis. Medical Hypotheses, 14, 1-19.

Scherrer, U., Pryor, S.L., Bertocci, L.A., & Victor, R.G. (1990). Arterial baroreflex buffering of sympathetic activation during exercise-induced elevations in arterial pressure. Journal of Clinical Investigation, 86, 1855-1861.

Schmidt, M., Ledderhas, C., & Honig, A. (1985). Kidney function during arterial chemoreceptor stimulation. Influence of unilateral renal nerve section, bilateral cervical vagotomy, constant artificial ventilation and carotid body inactivation. Biomedica Biochimica Acta, 44, 695-709.

Schuit, A.J., van Amelsvoort, L.G., Verheij, T.C., Rijneke, R.D., Maan, A.C., Swenne, C.A., & Schouten, E.G. (1999). Exercise training and heart rate variability in older people. Medicine and Science in Sports and Exercise, 31, 816-821.

Schwartz, J.B., Gibb, W.J., & Tran, T. (1991). Aging effects on heart rate variation. Journal of Gerontology: Medical Sciences, 46, M99- M106.

Schwartz, P.J. (1998). The autonomic nervous system and sudden death. European Heart Journal, 19, (Supp. F), F72-F80.

Schwartz, P.J., & Vanoli, E. (1981). Cardiac arrhythmias elicited by interaction between acute myocardial ischemia and sympathetic hyperactivity: a new experimental model for the study of antiarrhythmic drugs. Journal of Cardiovascular Pharmacology, 3, 1251-1259.

Schwartz, P.J., Locati, E.H., Moss, A.J., Crampton, R.S., Trazzi, R., & Ruberti, U. (1991). Left cardiac sympathetic denervation in the therapy of the congenital long QT syndrome: a worldwide report. Circulation, 84, 503-511.

Schwartz, P.J., Motolese, M., Pollavini, G., Lotto, A., Ruberti, U., Trazzi, R., Bartorelli, C., Zanchetti, A., & The Italian Sudden Death Prevention Group. (1992). Prevention of sudden cardiac death after a first myocardial infarction by pharmacologic or surgical antiadrenergic interventions. Journal of Cardiovascular Electrophysiology, 3, 2-16.

Schwartz, R., Jaeger, L., Veith, R., & Lakshminarayan, S. (1990). The effect of diet or exercise on plasma norepinephrine kinetics in moderately obese young men. International Journal of Obesity, 14, 1-11.

Seals, D.R. (1991). Sympathetic neural adjustments to stress in physically trained and untrained humans. Hypertension, 17, 36-43.

Seals, D.R., & Chase, P.B. (1989). Influence of physical training on heart rate variability and baroreflex circulatory control. Journal of Applied Physiology, 66, 1886-1895.

Sekiguchi, C., Handa, Y., Gotoh, M, Kurihara, Y., Nagasawa, Y., & Kuroda, I. (1979). Frequency analysis of heart rate variability under flight conditions. Aviation Space and Environmental Medicine, 50, 625-634.

Shahani, B.T., Halperin, J.J., Boulu, P., & Cohen, J. (1984). Sympathetic skin response: a method of assessing unmyelinated axon dysfunction in peripheral neuropathies. Journal of Neurology, Neurosurgery, and Psychiatry, 47, 536-542.

Shannon, D.C., Carley, D.W., & Benson, H. (1987). Aging modulation of heart rate. American Journal of Physiology, 253, H874-H877.

Sheldahl, L.M., Ebert, T.J., Cox, B., & Tristani, F.E. (1994). Effect of aerobic training on baroreflex regulation of cardiac and sympathetic function. Journal of Applied Physiology, 76, 158-165.

Sheriff, D.D., O'Leary, D.S., Scher, A.M., & Rowell, L.B. (1990). Baroreflex attenuates pressor response to graded muscle ischemia in exercising dogs. American Journal of Physiology, 258, H305-H310.

Sheriff, D.D., Wyss, C.R., Rowell, L.B., & Scher, A.M. (1987). Does inadequate oxygen delivery trigger pressor response to muscle hypoperfusion during exercise? American Journal of Physiology, 253, H1199-H1207.

Sherwood, A., Hinderliter, A.L., & Light, K.C. (1995). Physiological determinants of hyperreactivity to stress in borderline hypertension. Hypertension, 25, 384-390.

Sherwood, A., Light, K.C., & Blumenthal, J.A. (1989). Effects of aerobic exercise training on hemodynamic responses during psychosocial stress in normaotensive and borderline hypertensive type A men: a preliminary report. Psychosomatic Medicine, 51, 123-136.

Sherwood, A., May, C.W., Siegal, W.C., & Blumenthal, J.A. (1995). Ethnic differences in hemodynamic responses to stress in hypertensive men and women. American Journal of Hypertension, 8, 552-557.

Shi, X.G., Anderson, J.M., Potts, J.T., Foresman, B.H., Stern, S.A., & Raven, P.B. (1993). Aortic baroreflex control of heart rate during hypertensive stimuli: effect of fitness. Journal of Applied Physiology, 74, 1555-1562.

Shi, X.G., Crandall, C.G., Potts, J.T., Williamson, J.W., Foresman, B.H., & Raven, P.B. (1993). A diminished aortic-cardiac reflex during hypotension in aerobically fit young men. Medicine and Science in Sports and Exercise, 25, 1024-1030.

Shi, X., Squires, W.G., Williamson, J.W., Crandall, C.G., Chen, J., Krock, L.P., & Raven, P.B. (1992). Aerobic fitness: I. Response of volume regulating hormaones to head-down tilt. Medicine and Science in Sports and Exercise, 24, 991-998.

Shin, K., Minamitani, H., Onishi, S., Yamazaki, H., & Lee, M. (1997). Autonomic differences between athletes and nonathletes: spectral analysis approach. Medicine and Science in Sports and Exercise, 29, 1482-1490.

Shulhan, D., Scher, H., & Furedy, J.J. (1986). Phasic cardiac reactivity to psychological stress as a function of aerobic fitness level. Psychophysiology, 23, 562-566.

Sinnreich, R., Kark, J.D., Friedlander, Y., Sapoznikov, D., & Luria, M.H. 1998). Five minute recordings of heart rate variability for population studies: repeatability and age-sex characteristics. Heart, 80, 156-162.

Sinyor, D., Peronnet, F., Brisson, G., & Seraganian, P. (1988). Failure to alter sympathoadrenal response to psychosocial stress following aerobic training. Physiology and Behavior, 42, 293-296.

Sinyor, D., Golden, M., Steinert, Y., & Seraganian, P. (1986). Experimental manipulation of aerobic fitness and the response to psychosocial stress: heart rate and self-report measures. Psychosomatic Medicine, 48, 324-337.

Sinyor, D., Schwartz, S.G., Peronnet, F., Brisson, G., & Seraganian, P. (1983). Aerobic fitness level and reactivity to psychological stress: physiological, biochemical, and subjective measures. Psychosomatic Medicine, 45, 205-217.

Sleight, P. (1997). The importance of the autonomic nervous system in health and disease. Australian and New Zealand Journal of Medicine, 27, 467-473.

Sloan, R.P., De Meersman, R.E., Shapiro, P.A., Bagiella, E., Kuhl, J.P., Zion, A.S., Paik, M., & Myers, M.M. (1997). Cardiac autonomic control is inversely related to blood pressure variability responses to psychological challenge. American Journal of Physiology, 272, H2227-H2232.

Smith, J.J., & Kampine, J.P. (1990). Circulatory Physiology – the essentials. (pp.144-178). Baltimore: Williams and Wilkins.

Smith, M.L., Graitzer, H.M., Hudson, D.L., & Raven, P.B. (1988). Baroreflex function in endurance- and static exercise-trained men. Journal of Applied Physiology, 64, 585-591.

Smith, M.L., Hudson, D.L., Graitzer, H.M., & Raven, P.B. (1989). Exercise training bradycardia: the role of autonomic balance. Medicine and Science in Sports and Exercise, 21, 40-44.

Smith, O.A., Rushner, R.F., & Lasher, E.P. (1960). Similarity of cardiovascular responses to exercise and to diencephalic stimulation. American Journal of Physiology, 198, 1139-1142.

Smith, S.A., Querry, R.G., Fadel, P.J., Welch-O'Connor. R.M., Olivencia-Yurvati, A., Shi, X., & Raven, P.B. (2000). Differential baroreflex control of heart rate in sedentary and aerobically fit individuals. Medicine and Science in Sports and Exercise, 32, 1419-1430.

Smith, S.A., Stallard, T.J., Salih, M.M., & Littler, W.A. (1987). Can sinoaortic baroreceptor heart reflex sensitivity be determined from phase IV of the Valsalva manoeuvre? Cardiovascular Research, 21, 422-427.

Smyth, H.S., Sleight, P., & Pickering, G.W. (1969). Reflex regulation of arterial pressure during sleep in man: a quantitative method of assessing baroreflex sensitivity. Circulation Research, 24, 109-121.

Soliven, B., Maselli, R., Jaspan, J., Green, A., Graziano, H., Petersen, M., & Spire, J.P. (1987). Sympathetic skin response in diabetic neuropathy. Muscle and Nerve, 10, 711-716.

Sothmann, M.S., Hart, B.A., & Horn, T.S. (1992). Sympathetic nervous system and behavioral responses to stress following exercise training. Physiology and Behavior, 51, 1097-1103.

Sothmann, M.S., Horn, T.S., Hart, B.A., & Gustafson, A.B. (1987). Comparison of discrete cardiovascular fitness groups on plasma catecholamine and selected behavioral responses to psychological stress. Psychophysiology, 24, 47-54.

Soto, L.F., Kikuchi, D.A., Arcilla, R.A., Savage, D.D., & Berenson, G.S. (1989). Echocardiographic functions and blood pressure levels in children and young adults from a biracial population: the Bogalusa Heart Study. American Journal of the Medical Sciences, 296, 271-279.

Sowers, J.R., Rubenstein, L.Z., & Stern, N. (1983). Plasma norepinephrine responses to posture and isometric exercise increase with age in the absence of obesity. Journal of Gerontology, 38, 315-317.

Spalding, T.W., Jeffers, L.S., Porges, S.W., & Hatfield, B.D. (2000). Vagal and cardiac reactivity to psychological stressors in trained and untrained men. Medicine and Science in Sports and Exercise, 32, 581-591.

Spina, R.J. (1999). Cardiovascular adaptations to endurance exercise training in older men and women. Exercise and Sport Sciences Reviews, 27, 317-332.

Stahle, A., Nordlander, R., & Bergfeldt, L. (1999). Aerobic group training improves exercise capacity and heart rate variability in elderly patients with a recent coronary event. European Heart Journal, 20, 1638-1646.

Stein, P.K., & Boutcher, S.H. (1992). The effect of participation in an exercise training program on cardiovascular reactivity in sedentary middle-aged males. International Journal of Psychophysiology, 13, 215-223.

Stein, P.K., Ehsani, A.A., Domitrovich, P.P., Kleiger, R.E., & Rottman, J.N. (1999). Effect of exercise training on heart rate variability in healthy older adults. American Heart Journal, 138, 567-576.

Steptoe, A., Moses, J., Mathews, A., & Edwards, S. (1990). Aerobic fitness, physical activity, and psychophysiological reactions to mental tasks. Psychophysiology, 27, 264-274.

Stevens, G.H.J., Foresman, B.H., Shi, X., Stern, S.A., & Raven, P.B. (1992). Reduction in LBNP tolerance following prolonged endurance exercise training. Medicine and Science in Sports and Exercise, 24, 1235-1244.

Stratton, J.R., Cerquerira, M.D., Schwartz, R.S., Levy, W.C., Veith, R.C., Kahn, S.E., & Abrass, I.B. (1992). Differences in cardiovascular responses to isoproterenol in relation to age and exercise training in healthy men. Circulation, 86, 504-512.

Sun, J.C.L., Elken, O., & Mekjavic, I.B. (1993). Autonomic control of heart rate during blood flow restricted exercise in man. European Journal of Applied Physiology, 66, 202-206.

Sundlof, G., & Wallin, B.G. (1977). The variability of muscle nerve sympathetic activity in resting recumbent man. Journal of Physiology, 272, 383-397.

Sundlof, G., & Wallin, B.G. (1978). Human muscle nerve sympathetic activity at rest. Relationship to blood pressure and age. Journal of Physiology, 274, 621-637.

Surks, M.L., Beckwitt, H.J., & Chidsey, C.A. (1967). Changes in plasma thyroxine concentration and metabolism catecholamine excretion and basal oxygen consumption during

acute exposure to high altitude. Journal of Clinical Endocrinology and Metabolsm, 27, 789-799.

Svedenhag, J., Martinsson, A., Ekblom, B., & Hjemdahl, P. (1986). Altered cardiovascular responsiveness to adrenaline in endurance-trained subjects. Acta Physiologica Scandinavica, 126, 539-550.

Svedenhag, J., Wallin, B.G., Sundlof, G., & Henriksson, J. (1984). Skeletal muscle sympathetic activity at rest in trained and untrained subjects. Acta Physiologica Scandinavica, 120, 499-504.

Swain, A., & Suls, J. (1996). Reproducibility of blood pressure and heart rate reactivity: a meta-analysis. Psychophysiology, 33, 162-174.

Szabo, A., Peronnet, F., Frenkl, R., Farkas, A., Petrekanits, M., Meszaros, J., Hetenyi, A., & Szabos, T. (1994). Blood pressure and heart rate reactivity to mental strain in adolescent judo athletes. Physiology and Behavior, 56, 219-224.

Takalo, R., Korhonen, I., Turjanmaa, V., Majahalme, S., Tuomisto, M., & Uusitalo, A. (1994). Short-term variability of blood pressure and heart rate in borderline and mildly hypertensive subjects. Hypertension, 23, 18-24.

Talmon, W.T., & Kelkar, P. (1993). Neural control of the heart – central and peripheral. Neurologic Clinics, 11, 239-256.

Task Force of the European Society of Cardiology & the North American Society of Pacing and Electrophysiology. (1996). Heart rate variability - standards of measurement, physiological interpretation, and clinical use. Circulation, 93, 1043-1065.

Taverner, D., Nunan, T.A., & Tonkin, A.L. (1996). Reproducibility of conventional and power spectral measurements of cardiovascular sympathetic activation in normal subjects. Clinical and Experimental Pharmacology and Physiology, 23, 804-806.

Taylor, J.A., Hand, G.A., Johnson, D.G., & Seals, D.R. (1992). Augmented forearm vasoconstriction during dynamic exercise in healthy older men. Circulation, 86, 1789-1799.

Tipton, C.M., Matthes, R.D., & Bedford, T.G. (1982). Influence of training on the blood pressure changes during lower body negative pressure in rats. Medicine and Science in Sports and Exercise, 14, 81-90.

Tollan, A., Oina, P., Kjelden, S.E., Eida, I., & Maltass, J.M. (1993). Progesterone reduces sympathetic tone without blood pressure or fluid balance in men. Gynecologic and Obstetric Investigation, 36, 234-238.

Torebjork, H.E. (1974). Afferent C units responding to mechanical, thermal, and chemical stimuli in human nonglabrous skin. Acta Physiologica Scandinavica, 92, 374-390.

Treiber, F.A., Musante, L., Braden, D., Arensman, F., Strong, W.B., Levy, M., & Leverett, S. (1990). Racial differences in hemodynamic responses to the cold face stimulus in children and adults. Psychosomatic Medicine, 52, 286-296.

Turner, J.R., Carroll, D., Costello, M., & Sims, J. (1988). The effects of aerobic fitness on additional heart rates during active psychological challenge. Journal of Psychophysiology, 2, 91-97.

Urata, H., Tanabe, Y., & Kiyonaga, A. (1987). Antihypertensive and volume-depleting effects of mild exercise on essential hypertension. Hypertension, 9, 245-252.

Urbina, E.M., Bao, W., Pickoff, A.S., & Berenson, G.S. (1998). Ethnic (black-white) contrasts in heart rate variability during cardiovascular reactivity testing in male adolescents with high and low blood pressure: The Bogalusa Heart Study. American Journal of Hypertension, 11, 196-202.

Van Brummelen, P., Buhler, F.R., Kiowski, W., & Amann, F.W. (1981). Age-related decrease in cardiac and peripheral vascular responsiveness to isoprenaline: studies in normal subjects. Clinical Science, 60, 571-577.

Van den Hombergh, C.E.J., Dekker, J.M., & Schouten, E.G. (1995). Short-term heart rate variability and physical activity in Dutch women and men aged 65-85. Cardiology in the Elderly, 3, 193-198.

Van Doornen, L.J.P., & De Geus, E.J.C. (1989). Aerobic fitness and the cardiovascular response to stress. Psychophysiology, 26, 17-28.

Van Egeren, L.F., & Sparrow, A.W. (1989). Laboratory stress testing to assess real life cardiovascular reactivity. Psychosomatic Medicine, 51, 1-9.

Van Faassen, I., Popp-Snijders, C., Nauta, J.J.P., Van Zijderveld, G.A., Van Doornen, L.J.P., & Tilders, F.J.H. (1992). Platelet catecholamine contents as related to trait anxiety and aerobic fitness. American Journal of Physiology, 263, E245-E249.

Van Hoogenhuyze, D., Weinstein, N., Martin, G.J., Weiss, J.S., Schaad, J.W., Sahyouni, X.N., Fintel, D., Remme, W.J., & Singer, D.H. (1991). Reproducibility and relation to mean heart rate of heart rate variability in normal subjects and in patients with congestive heart failure secondary to coronary artery disease. American Journal of Cardiology, 68, 1668-1676.

Vanoli, E., De Ferrari, G.M., Stramba-Badiale, M., Hull, S.S. Jr., Foreman, R.D., & Schwartz, P.J. (1991). Vagal stimulation and prevention of sudden death in conscious dogs with a healed myocardial infarction. Circulation Research, 68, 1471-1481.

Vatner, S.F., & McRitchie, R.J. (1975). Interaction of the chemoreflex and the pulmonary inflation reflex in the regulation of coronary circulation in conscious dogs. Circulation Research, 37, 664-673.

Verrier, R.L., & Lown, B. (1978). Sympathetic-parasympathetic interactions and ventricular electrical stability. In P.J. Schwartz, A.M. Brown, A. Malliani, & A. Zanchetti (Eds.), Neural Mechanisms in Cardiac Arrhythmias (pp. 75-85). New York: Raven Press.

Vestal, R.E., Wood, A.J.H., & Shand, D.G. (1979). Reduced beta-adrenoreceptor sensitivity in the elderly. Clinical Pharmacology and Therapeutics, 26, 181-186.

Victor, R.G., & Seals, D.R. (1989). Reflex stimulation of sympathetic outflow during rhythmic exercise in humans. American Journal of Physiology, 257, H2017-H2024.

Victor, R.G., Seals, D.R., & Mark, A.L. (1987). Differential control of heart rate and sympathetic nerve activity during dynamic exercise. Journal of Clinical Investigation, 79, 508-516.

von During, M., Andres, K.H., & Schmidt, R.F. (1984). Ultrastructure of fine afferent fibre terminators in muscle and tendon of the cat. In W. Hamann, & A. Iggo (Eds.), Sensory Receptor Mechanisms (pp. 15-23). Singapore: World Scientific Publications Company.

Voors, A.W., Webber, I.S., & Berenson, G.S. (1980). Racial contrasts in cardiovascular response to tests for children from a total community. Hypertension, 2, 686-694.

Waddington, J.L., MacCulloch, M.J., & Sambrooks, J.E. (1979). Resting heart rate variability in man declines with age. Experientia, 35, 1197-1198.

Waldrop, T.G., Rybicki, K.J., & Kaufman, M.P. (1984). Chemical activation of group I and II muscle afferents has no cardiorespiratory effects. Journal of Applied Physiology, 56, 1223-1228.

Wallin, B. G., Sundlof, G., Eriksson, B. M., Dominiak, P., Grobecker, H. & Lindblad, L. E. (1981). Plasma noradrenaline correlates to sympathetic muscle nerve activity in normotensive man. Acta Physiologica Scandinavica, 111, 69-73.

Wallin, B.G., Victor, R.G., & Mark, A.L. (1989). Sympathetic outflow to resting muscles during static handgrip and postcontraction muscle ischemia. American Journal of Physiology, 256, H105-H110.

Walsh, R.R. (1969). Heart rate and its neural regulation with rising body temperature in anaesthetized rats. American Journal of Physiology, 217, 1139-1143.

Warren, J.H., Jaffe, R.S., Wraa, C.E., & Stebbins, C.L. (1997). Effect of autonomic blockade on power spectrum of heart rate variability during exercise. American Journal of Physiology, 273, R495-R502.

Wilder, J. (1957). The Law of Initial Values in neurology and psychiatry. Journal of Nervous and Mental Disease, 125, 73-86.

Williamson, J.W., Nobrega, A.C.L., Winchester, P.K., Zim, S., & Mitchell, J.H. (1995). Instntaneous heart rate increase with dynamic exercise: central command and muscle-heart reflex contributions. Journal of Applied Physiology, 78, 1273-1279.

Williamson, J.W., & Raven, P.B. (1994). Unilateral carotid-cardiac baroreflex responses in exercise trained and untrained men. Medicine and Science in Sports and Exercise, 26, 217-223.

Winder, W.W., Hagberg, J.M., Hickson, R.C., Ehsani, A.A., & McLane, J.A. (1978). Time course of sympathoadrenal adaptation to endurance exercise training in man. Journal of Applied Physiology, 45, 370-374.

Winder, W.W., Hickson, R.C., Hagberg, J.M., Ehsani, A.A., & McLane, J.A. (1979). Training-induced changes in hormonal and metabolic responses to submaximal exercise. Journal of Applied Physiology, 46, 766-771.

Wyss, C.R., Ardell, J.L., Scher, A.M., & Rowell, L.B. (1983). Cardiovascular responses to graded reductions in hindlimb perfusion in exercising dogs. American Journal of Physiology, 245, H481-H486.

Yamada, Y., Miyajima, E., Tochikubo, O., Hatsukawa, T., & Ishii, M. (1989). Age-related changes in muscle sympathetic nerve activity in essential hypertension. Hypertension, 13, 870-877.

Yamamoto, Y., Hughson, R.L., & Peterson, J.C. (1991). Autonomic control of heart rate during exercise studied by heart rate variability spectral analysis. Journal of Applied Physiology, 71, 1136-1142.

Yataco, A.R., Fleisher, L.A., & Katzel, L.I. (1997). Heart rate variability and cardiovascular fitness in senior athletes. The American Journal of Cardiology, 80, 1389-1391.

Yin, F.C.P., Spurgeon, H.A., Greene, H.L., Lakatta, E.G., & Weisfeldt, M.L. (1979). Age-associated decrease in heart rate response to isoproterenol in dogs. Mechanisms of Ageing and Development, 10, 17-25.

Yin, F.C.P., Weisfeldt, M.L., & Milnor, W.R. (1981). Role of aortic input impedance in the decreased cardiovascular response to exercise with aging in dogs. Journal of Clinical Investigation, 68, 28-38.

Yokota, T., Matsunaga, T., Okiyama, R., Hirose, K., Tanabe, H., Furukawa, T., & Tsukagoshi, H. (1991). Sympathetic skin response in patients with multiple sclerosis compared with patients with spinal cord transection and normal controls. Brain, 114, 1381-1394.

Yusuf, S., & Teo, K.K. (1991). Approaches to prevention of sudden death: need for fundamental reevaluation. Journal of Cardiovascular Electrophysiology, 2, (Supp.), S233-S239.

Appendix B

Consent Form

CONSENT FORM

1. **Study Title:** Time Course of Alterations in Cardiac Autonomic Modulation Induced by Endurance Exercise Training

2. **Performance Sites:** Huey P. Long Field House, Dept. of Kinesiology, Cardiopulmonary Physiology Laboratory, Louisiana State University.

3. **Contacts:** The following investigators are available for questions at the telephone numbers and email addresses listed below:

Principal Investigator:

Robert H. Wood, Ph.D.	(225) 578-9142
Department of Kinesiology	rwood@lsu.edu

Co-Investigators:

C. Matthew Lee, B.S.	(225) 578-2036
Department of Kinesiology	clee11@lsu.edu
Michael Welsch, Ph.D.	(225) 578-9143
Department of Kinesiology	mwelsch@lsu.edu

4. **Purpose of the Study:** The purpose of this investigation will be to examine the time course of EKG changes induced by 2 weeks of exercise training.

5. **Subjects**:
A. Inclusion Criteria: All volunteers will be healthy adults without any overt signs of disease such as diabetes, heart disease, high blood pressure, or lung problems.
B: Exclusion Criteria: Individuals with any current medical problems (including those listed above) or infection. Any individual on medication known to affect the heart and blood vessels.
C: Maximum Number of Subjects: A total of 30 volunteers between the ages of 18 and 30 will be asked to participate in this study.

6. **Study Procedures**: The proposed study consists of either 6 or 10 visits to the laboratory over a 2-week period. Each visit is expected to last approximately 60-90 minutes.

Session one: During this session, the experiment will be explained to the participant and written informed consent will be obtained. The participant will also be asked to answer questions regarding his health history and history of physical activity. The participant will be measured for height and weight and body fat percent will be estimated using "skin-fold" techniques. The participant will then be asked to lie on an examination table while investigators will be collecting EKG data, which will require

the placement of three electrodes on the participant's torso. EKG data will be collected for 5-minutes as the participant continues to breathe at a comfortable rate and also during a subsequent 5-minute period in which the participant will be asked to breathe in such a fashion that they inhale and exhale once every 5 seconds. Lastly, the participant will ride a stationary bicycle while the investigators gradually increase the resistance against which the participant is working until either the participant asks to stop or the investigators determine that the test should be stopped. Throughout the bicycle test the participant will be asked to breathe through a mouthpiece, and the investigators will obtain measurements of heart rate and rhythm by analyzing the participant's "EKG" and blood pressure using a standard blood pressure cuff. Following this session, participants will be assigned to one of two treatment groups:

Group 1. Will engage in cycling exercise four times per week (Monday, Tuesday, Thursday, and Friday) for the subsequent two weeks
Group 2. Will serve as a control group and be asked not to alter their previous level of physical activity for the subsequent two weeks

Participants in both groups will then be asked to report to the laboratory 4 times during the subsequent 2 weeks (Monday and Thursday). During these sessions EKG data will be collected (as previously described) for 5-minutes as the participant rests in a supine position and breathes at a comfortable rate and then during a 5-minute period in which the participant will be asked to breathe in such a fashion that they inhale and exhale once every 5 seconds.
Participants in Group 1 will additionally be asked to engage in exercise on a stationary bicycle following the EKG collection. Furthermore, Group 1 participants will be asked to report to the laboratory on Tuesday and Friday for an identical exercise session. This exercise will consist of the participant riding a stationary bicycle for 40-minutes which will be divided into three periods described below.

- 5-minutes of cycling with no added resistance.
- *30-minutes of cycling at an intensity equal to approximately 80-85% of the participant's* maximal capacity.
- 5-minutes of cycling with no added resistance.

Post-testing session: The post-testing session will take place on the following Monday. This session will be a replication of *session one*.

7. Benefits: Participation in this study may provide a few benefits to the participants. These include the health benefits associated with regular physical exercise and the acquisition of information regarding the participant's level of physical fitness.

8. Risks/Discomforts: There is minimal risk associated with the above procedures. The risks are as follows:

Exercise Testing/Training: The risks of exercise testing and training include heightened heart rate and blood pressure, muscle soreness or stiffness, muscle injuries, heart attack, stroke, and in rare instances, death. Studies of exercise testing in healthy populations reveal one hospitalization per 187,500 tests (0.001%).

Blood Pressure: There are no real risks associated with the measurement of blood pressure. However, in rare instances some participants report discomfort when having blood pressure measured. Therefore, if the participant desires to stop the blood pressure measurement, the cuff will be removed immediately.

9. **Measures Taken to Reduce Risk:** The risks in this study will be minimized as a result of proper evaluation, education, and appropriate assessment of the responses to exercise and the presence of well-trained personnel capable of and experienced in monitoring responses to exercise.

10. **Right to Refuse:** Participation in this study is completely voluntary and participants may withdraw at any time without penalty.

11. **Privacy:** Though the results of this study may be published, the privacy of participants will be protected and their identities will remain confidential. All subject records will be kept in a locked file located in a secured lab. The only persons with entry into the laboratory will be the investigators. No publication arising as the result of this investigation will indicate the names or identities of the participants. Thus, participant data will be kept confidential unless release is legally compelled.

12. **Financial Information:** There is no monetary cost to participate in this study nor will any payment be rendered to participants.

13. **Withdrawal:** Participants may voluntarily withdraw from this study at any time without penalty. The participant's records, however, will be kept with those of others in a locked file in a secured laboratory.

14. **Removal:** Participants may be removed from the study under the investigators discretion. Conditions warranting removal from the study include: a) fulfillment of all of the study requirements, b) failure of the participant to comply with the requirements of the study, and/or c) the participant developing a condition listed in the exclusion criteria.

The study has been discussed with me and all my questions have been answered. I may direct additional questions regarding study specifics to Robert H. Wood, Ph.D. (225) 578-9142. If I have questions about subjects' rights or other concerns, I can contact Robert C. Mathews, Chairman, LSU Institutional Review Board, (225) 578-8692. I agree to participate in the study described above and acknowledge the researchers' obligation to provide me with a copy of this consent form if signed by me.

_____

Participant's signature Date

_____

Witness signature Date

_____

Investigator's signature Date

Appendix C

SAS Programs

Program C.1

Program for Independent T-Test on Age and Height

```
dm 'log;clear;out;clear';
data X;
input group depvar;
cards;

;
proc ttest data=X;
class group;
var depvar;
run;
quit;
```

Program C.2

Program for Repeated Measures ANOVA on Descriptive or Physiological Indices

```
dm 'log;clear;out;clear';
data X;
input subj group $ pre post;
cards;

;
proc glm data=X;
class group;
model pre post = group / nouni;
repeated time 2 (0 1);
means group;
run;
proc means data=X mean std;
class group;
var pre post;
run;
quit;
```

Program C.3

Program to Test for Simple Effects of Descriptive or Physiological Indices

```
dm 'log;clear;out;clear';
data X;
infile cards missover;
input pre post;
cards;

;
proc means data=X;
run;
Proc glm data=X;
model pre post =/ nouni;
repeated time 2 contrast (1) / summary;
run;
quit;
```

Program C.4

Program for Repeated Measures ANOVA on HRV or Arterial Pressure During Each Testing Session

```
dm 'log;clear;out;clear';
data X;
input group pb sb tilt after;
cards;

;
proc sort data=X;
by group;
run;
proc means data=X mean std;
by group;
run;
proc glm data=X;
class group;
model pb sb tilt after = group / nouni;
repeated time 4 contrast (1) / summary;
repeated time 4 contrast (2) / summary;
repeated time 4 contrast (3) / summary;
run;
quit;
```

Program C.5

Program to Test for Simple Effects of HRV or Arterial Pressure Variables During Each Testing Session

```
dm 'log;clear;out;clear';
data X;
infile cards missover;
input cond1-cond4;
cards;

;
proc means data=X;
run;
proc glm data=X;
model cond1-cond4 =/ nouni;
repeated time 4 contrast (1) / summary;
repeated time 4 contrast (2) / summary;
repeated time 4 contrast (3) / summary;
run;
quit;
```

Program C.6

Program for Repeated Measures ANOVA on HRV or Arterial Pressure Variables During Each Condition

```
dm 'log;clear;out;clear';
data X;
input group T1 T2 T3 T4 T5;
cards;

;
proc sort data=X;
by group;
run;
proc means data=X mean std;
by group;
run;
proc glm data=X;
class group;
model T1 T2 T3 T4 T5 = group / nouni;
repeated time 5 contrast (1) / summary;
run;
quit;
```

Program C.7

Program to Test for Simple Effects of HRV or Arterial Pressure Variables During Each Condition

```
dm 'log;clear;out;clear';
data X;
infile cards missover;
input test1-test5;
cards;

;
proc means data=X;
run;
proc glm data=X;
model test1-test5 =/ nouni;
repeated time 5 contrast (1) / summary;
run;
quit;
```

Appendix D

ANOVA Tables

Table D.1

ANOVA Summary Table for Body Weight

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	46611.98			
Group (A)	1	652.69	652.69	0.31	0.5818
Residual between	22	45959.29	2089.06		
Within subjects	24	19.5			
Time (B)	1	2.52	2.52	3.84	0.0630
A X B Interaction	1	2.52	2.52	3.84	0.0630
Residual within	22	14.46	0.6572		
Total	47	46631.48			

Table D.2

ANOVA Summary Table for the Sum of Skinfolds

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	93354.31			
Group (A)	1	5271.02	5271.02	1.32	0.2635
Residual between	22	88083.29	4003.79		
Within subjects	24	1175.5			
Time (B)	1	256.69	256.69	6.8	0.0161
A X B Interaction	1	88.02	88.02	2.33	0.1411
Residual within	22	830.79	37.76		
Total	47	94529.81			

Table D.3

ANOVA Summary Table for Percent Body Fat

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1507.85			
Group (A)	1	73.71	73.71	1.13	0.2992
Residual between	22	1434.14	65.19		
Within subjects	24	16.36			
Time (B)	1	4.13	4.13	8.21	0.0090
A X B Interaction	1	1.17	1.17	2.32	0.1421
Residual within	22	11.06	0.5029		
Total	47	1524.21			

Table D.4

ANOVA Summary Table for the Physical Activity Questionnaire

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	20025703			
Group (A)	1	12668191.37	12668191.37	37.88	0.0001
Residual between	22	7357512.03	334432.37		
Within subjects	24	26745287			
Time (B)	1	13550253.96	13550253.96	5644.34	0.0001
A X B Interaction	1	13142219.09	13142219.09	5474.37	0.0001
Residual within	22	52814.99	2400.68		
Total	47	46770990			

Table D.5

ANOVA Summary Table for VO_2 ($ml \cdot kg^{-1} \cdot min^{-1}$) at Rest

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	103.88			
Group (A)	1	12.81	12.81	3.10	0.0924
Residual between	22	91.07	4.14		
Within subjects	24	39.1			
Time (B)	1	7.52	7.52	5.24	0.0320
A X B Interaction	1	0.03000	0.03000	0.02	0.8863
Residual within	22	31.55	1.43		
Total	47	142.98			

Table D.6

ANOVA Summary Table for VO_2 ($l \cdot min^{-1}$) at Rest

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.92272			
Group (A)	1	0.02862	0.0862	0.70	0.4104
Residual between	22	0.8941	0.04064		
Within subjects	24	0.254218			
Time (B)	1	0.04915	0.04915	5.29	0.0313
A X B Interaction	1	0.0007680	0.0007680	0.08	0.7764
Residual within	22	0.2043	0.009286		
Total	47	1.176938			

Table D.7

ANOVA Summary Table for V_E at Rest

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	590.71			
Group (A)	1	1.65	1.65	0.06	0.8062
Residual between	22	589.06	26.78		
Within subjects	24	138.22			
Time (B)	1	31.52	31.52	6.58	0.0177
A X B Interaction	1	1.30	1.30	0.27	0.6076
Residual within	22	105.40	4.79		
Total	47	728.93			

Table D.8

ANOVA Summary Table for RF at Rest

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	682.25			
Group (A)	1	6.75	6.75	0.22	0.6438
Residual between	22	675.50	30.70		
Within subjects	24	213.00			
Time (B)	1	33.33	33.33	4.37	0.0483
A X B Interaction	1	12.00	12.00	1.57	0.2227
Residual within	22	167.67	7.62		
Total	47	895.25			

Table D.9

ANOVA Summary Table for T_V at Rest

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	3.1538			
Group (A)	1	0.001801	0.001801	0.01	0.9118
Residual between	22	3.152	0.1433		
Within subjects	24	1.0617			
Time (B)	1	0.3034	0.3034	8.81	0.0071
A X B Interaction	1	0.0004201	0.0004201	0.01	0.9131
Residual within	22	0.7579	0.03445		
Total	47	4.2155			

Table D.10

ANOVA Summary Table for VCO_2 at Rest

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.6754			
Group (A)	1	0.002700	0.002700	0.09	0.7691
Residual between	22	0.6727	0.03058		
Within subjects	24	0.2341			
Time (B)	1	0.07053	0.07053	9.49	0.0055
A X B Interaction	1	0.00000833	0.00000833	0.00	0.9736
Residual within	22	0.1636	0.007434		
Total	47	0.9095			

Table D.11

ANOVA Summary Table for RQ at Rest

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.36442			
Group (A)	1	0.06092	0.06092	4.42	0.0473
Residual between	22	0.3035	0.01380		
Within subjects	24	0.1728			
Time (B)	1	0.005002	0.005002	0.66	0.4247
A X B Interaction	1	0.001519	0.001519	0.20	0.6584
Residual within	22	0.1663	0.007560		
Total	47	0.5372			

Table D.12

ANOVA Summary Table for Heart Rate at Rest

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	7852.98			
Group (A)	1	892.69	892.69	2.82	0.1072
Residual between	22	6960.29	316.38		
Within subjects	24	1339.5			
Time (B)	1	17.52	17.52	0.29	0.5931
A X B Interaction	1	11.02	11.02	0.18	0.6713
Residual within	22	1310.96	59.59		
Total	47	9192.48			

Table D.13

ANOVA Summary Table for VO_2 ($ml \cdot kg^{-1} \cdot min^{-1}$) During Peak Exercise

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	397.11			
Group (A)	1	27.30	27.30	1.62	0.2158
Residual between	22	369.81	16.81		
Within subjects	24	112.42			
Time (B)	1	5.60	5.60	1.96	0.1750
A X B Interaction	1	44.08	44.08	15.46	0.0007
Residual within	22	62.74	2.85		
Total	47	509.53			

Table D.14

ANOVA Summary Table for VO_2 ($l \cdot min^{-1}$) During Peak Exercise

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	10.012			
Group (A)	1	0.2595	0.2595	0.59	0.4524
Residual between	22	9.752	0.4433		
Within subjects	24	0.8163			
Time (B)	1	0.01972	0.01972	0.83	0.3728
A X B Interaction	1	0.2723	0.2723	11.42	0.0027
Residual within	22	0.5243	0.0238		
Total	47	10.83			

Table D.15

ANOVA Summary Table for V_E During Peak Exercise

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	19157.9			
Group (A)	1	1691.00	1691.00	2.13	0.1586
Residual between	22	17466.90	793.95		
Within subjects	24	5180.88			
Time (B)	1	13.13	13.13	0.09	0.7727
A X B Interaction	1	1789.74	1789.74	11.66	0.0025
Residual within	22	3378.01	153.55		
Total	47	24338.78			

Table D.16

ANOVA Summary Table for RF During Peak Exercise

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	2330.48			
Group (A)	1	38.52	38.52	0.37	0.5494
Residual between	22	2291.96	104.18		
Within subjects	24	463.5			
Time (B)	1	2.52	2.52	0.13	0.7169
A X B Interaction	1	50.02	50.02	2.68	0.1160
Residual within	22	410.96	18.68		
Total	47	2793.98			

Table D.17

ANOVA Summary Table for T_V During Peak Exercise

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	18.1144			
Group (A)	1	0.3144	0.3144	0.39	0.5394
Residual between	22	17.80	0.8089		
Within subjects	24	1.553			
Time (B)	1	0.0002125	0.0002125	0.00	0.9524
A X B Interaction	1	0.2729	0.2729	4.68	0.0416
Residual within	22	1.28	0.05827		
Total	47	19.6675			

Table D.18

ANOVA Summary Table for VCO_2 During Peak Exercise

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	16.487			
Group (A)	1	0.5970	0.5970	0.83	0.3731
Residual between	22	15.89	0.7221		
Within subjects	24	2.735			
Time (B)	1	0.02516	0.02516	0.30	0.5899
A X B Interaction	1	0.8600	0.8600	10.22	0.0042
Residual within	22	1.85	0.08411		
Total	47	19.222			

Table D.19

ANOVA Summary Table for RQ During Peak Exercise

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.1923			
Group (A)	1	0.001519	0.001519	0.18	0.6796
Residual between	22	0.1908	0.008672		
Within subjects	24	0.08715			
Time (B)	1	0.0002521	0.0002521	0.07	0.7971
A X B Interaction	1	0.005002	0.005002	1.34	0.2588
Residual within	22	0.08190	0.003723		
Total	47	0.2795			

Table D.20

ANOVA Summary Table for Heart Rate During Peak Exercise

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	3730.31			
Group (A)	1	275.52	275.52	1.75	0.1989
Residual between	22	3454.79	157.04		
Within subjects	24	583.5			
Time (B)	1	6.02	6.02	0.24	0.6281
A X B Interaction	1	28.52	28.52	1.14	0.2966
Residual within	22	548.96	24.95		
Total	47	4313.81			

Table D.21

ANOVA Summary Table for the Mean RR Interval During Test 1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1318503.64			
Group (A)	1	81718.59	81718.59		
Residual between	22	1236785.05	56217.50	1.45	0.2408
Within subjects	72	1266651.98			
Time (B)	3	1003900.70	334633.57	95.51	0.0001
A X B Interaction	3	31509.94	10503.31	3.00	0.0368
Residual within	66	231241.34	3503.66		
Total	95	2585155.62			

Table D.22

ANOVA Summary Table for SDNN During Test 1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	54638.01			
Group (A)	1	1195.75	1195.75	0.49	0.4903
Residual between	22	53442.26	2429.19		
Within subjects	72	22094.69			
Time (B)	3	6240.19	2080.06	9.12	0.0001
A X B Interaction	3	800.24	266.75	1.17	0.3281
Residual within	66	15054.26	228.09		
Total	95	76732.7			

Table D.23

ANOVA Summary Table for lnTP During Test 1.

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	46.04			
Group (A)	1	2.0796	2.0796	1.04	0.3187
Residual between	22	43.96	1.998		
Within subjects	72	23.94			
Time (B)	3	4.782	1.594	5.67	0.0016
A X B Interaction	3	0.61723	0.2057	0.73	0.5363
Residual within	66	18.54	0.2809		
Total	95	69.98			

Table D.24

ANOVA Summary Table for lnLF During Test 1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	40.92			
Group (A)	1	0.5092	0.5092	0.28	0.6038
Residual between	22	40.413	1.837		
Within subjects	72	34.31			
Time (B)	3	1.762	0.5872	1.24	0.3021
A X B Interaction	3	1.309	0.4364	0.92	0.4352
Residual within	66	31.24	0.4733		
Total	95	75.23			

Table D.25

ANOVA Summary Table for lnHF During Test 1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	53.87			
Group (A)	1	2.510	2.510	1.07	0.3111
Residual between	22	51.36	2.335		
Within subjects	72	77.88			
Time (B)	3	73.17	24.39	60.28	0.0001
A X B Interaction	3	2.011	0.6703	1.66	0.1848
Residual within	66	26.70	0.4046		
Total	95	131.75			

Table D.26

ANOVA Summary Table for lnLF/lnHF During Test 1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.8655			
Group (A)	1	0.0277	0.0277	0.73	0.4027
Residual between	22	0.8378	0.0381		
Within subjects	72	5.59			
Time (B)	3	4.001	1.333	56.02	0.0001
A X B Interaction	3	0.01596	0.005318	0.22	0.8798
Residual within	66	1.5716	0.02381		
Total	95	6.45			

Table D.27

ANOVA Summary Table for lnLFNU During Test 1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	4.615			
Group (A)	1	0.1822	0.1822	0.90	0.3520
Residual between	22	4.4328	0.2015		
Within subjects	72	18.25			
Time (B)	3	11.95	3.984	42.48	0.0001
A X B Interaction	3	0.1074	0.0358	0.38	0.7664
Residual within	66	6.1903	0.09379		
Total	95	22.86			

Table D.28

ANOVA Summary Table for lnHFNU During Test 1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	7.569			
Group (A)	1	0.1969	0.1969	0.59	0.4515
Residual between	22	7.372	0.3351		
Within subjects	72	47.81			
Time (B)	3	34.19	11.40	55.78	0.0001
A X B Interaction	3	0.1399	0.04667	0.23	0.8763
Residual within	66	13.48	0.2043		
Total	95	55.38			

Table D.29

ANOVA Summary Table for lnHF/lnTP During Test 1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.2784			
Group (A)	1	0.002326	0.002326	0.19	0.6710
Residual between	22	0.2761	0.01255		
Within subjects	72	1.308			
Time (B)	3	0.9426	0.3142	59.13	0.0001
A X B Interaction	3	0.01502	0.005005	0.94	0.4255
Residual within	66	0.3507	0.005314		
Total	95	1.587			

Table D.30

ANOVA Summary Table for the Mean RR Interval During Test 2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1143664.0			
Group (A)	1	115492.73	115492.73	2.47	0.1302
Residual between	22	1028171.35	46735.06		
Within subjects	72	1414509.0			
Time (B)	3	1144857.07	381619.02	97.62	0.0001
A X B Interaction	3	11652.49	3884.16	0.99	0.4014
Residual within	66	257999.55	3909.08		
Total	95	2558173.1			

Table D.31

ANOVA Summary Table for SDNN During Test 2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	55689.57			
Group (A)	1	144.72	144.72	0.06	0.8130
Residual between	22	55544.85	2524.77		
Within subjects	72	34149.43			
Time (B)	3	11459.33	3819.78	11.80	0.0001
A X B Interaction	3	1320.97	440.32	1.36	0.2627
Residual within	66	21369.13	323.77		
Total	95	89839.00			

Table D.32

ANOVA Summary Table for lnTP During Test 2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	30.72			
Group (A)	1	0.08687	0.08687	0.06	0.8051
Residual between	22	30.63	1.39		
Within subjects	72	34.85			
Time (B)	3	9.80	3.267	8.84	0.0001
A X B Interaction	3	0.6488	0.2163	0.59	0.6269
Residual within	66	24.40	0.3697		
Total	95	65.57			

Table D.33

ANOVA Summary Table for lnLF During Test 2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	38.11			
Group (A)	1	0.002808	0.002808	0.00	0.9682
Residual between	22	38.11	1.73		
Within subjects	72	40.50			
Time (B)	3	10.51	3.504	7.81	0.0002
A X B Interaction	3	0.3799	0.1266	0.28	0.8381
Residual within	66	29.61	0.4487		
Total	95	78.61			

Table D.34

ANOVA Summary Table for lnHF During Test 2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	55.09			
Group (A)	1	0.9832	0.9832	0.40	0.5337
Residual between	22	54.11	2.459		
Within subjects	72	122.85			
Time (B)	3	88.52	29.51	58.04	0.0001
A X B Interaction	3	0.7739	0.2580	0.51	0.6785
Residual within	66	33.56	0.5084		
Total	95	177.95			

Table D.35

ANOVA Summary Table for lnLF/lnHF During Test 2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1.023			
Group (A)	1	0.01837	0.01837	0.40	0.5326
Residual between	22	1.005	0.04568		
Within subjects	72	5.65			
Time (B)	3	4.012	1.337	55.68	0.0001
A X B Interaction	3	0.0496	0.01654	0.69	0.5623
Residual within	66	1.59	0.024		
Total	95	6.675			

Table D.36

ANOVA Summary Table for lnLFNU During Test 2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	6.844			
Group (A)	1	0.2842	0.2842	0.95	0.3397
Residual between	22	6.56	0.2984		
Within subjects	72	24.09			
Time (B)	3	16.48	5.49	48.39	0.0001
A X B Interaction	3	0.1225	0.04083	0.36	0.7823
Residual within	66	7.492	0.1135		
Total	95	30.94			

Table D.37

ANOVA Summary Table for lnHFNU During Test 2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	6.619			
Group (A)	1	0.1644	0.1644	0.56	0.4621
Residual between	22	6.455	0.2934		
Within subjects	72	38.60			
Time (B)	3	28.34	9.45	62.18	0.0001
A X B Interaction	3	0.2305	0.0768	0.51	0.6797
Residual within	66	10.03	0.1519		
Total	95	45.22			

Table D.38

ANOVA Summary Table for lnHF/lnTP During Test 2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.2846			
Group (A)	1	0.0109	0.0109	0.87	0.3603
Residual between	22	0.2737	0.01244		
Within subjects	72	1.29			
Time (B)	3	0.9918	0.3306	74.15	0.0001
A X B Interaction	3	0.00499	0.00166	0.37	0.7727
Residual within	66	0.2943	0.004459		
Total	95	1.58			

Table D.39

ANOVA Summary Table for the Mean RR Interval During Test 3

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1142226.9			
Group (A)	1	85346.03	85346.03	1.78	0.1962
Residual between	22	1056880.99	48040.05		
Within subjects	72	1481470.0			
Time (B)	3	1170211.05	390070.35	87.00	0.0001
A X B Interaction	3	15329.75	5109.92	1.14	0.3396
Residual within	66	295929.28	4483.78		
Total	95	2623697.0			

Table D.40

ANOVA Summary Table for SDNN During Test 3

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	57036.66			
Group (A)	1	508.81	508.81	0.20	0.6607
Residual between	22	56527.85	2569.45		
Within subjects	72	48383.97			
Time (B)	3	7568.93	2522.98	4.16	0.0092
A X B Interaction	3	789.39	263.13	0.43	0.7294
Residual within	66	40025.65	606.45		
Total	95	105420.63			

Table D.41

ANOVA Summary Table for lnTP During Test 3

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	48.92			
Group (A)	1	0.08667	0.08667	0.04	0.8452
Residual between	22	48.83	2.22		
Within subjects	72	32.88			
Time (B)	3	2.339	0.7798	1.71	0.1743
A X B Interaction	3	0.3687	0.1229	0.27	0.8476
Residual within	66	30.17	0.4570		
Total	95	81.79			

Table D.42

ANOVA Summary Table for lnLF During Test 3

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	55.36			
Group (A)	1	0.01563	0.01563	0.01	0.9379
Residual between	22	55.34	2.52		
Within subjects	72	39.25			
Time (B)	3	3.848	1.2827	2.39	0.0763
A X B Interaction	3	0.02298	0.00766	0.01	0.9976
Residual within	66	35.38	0.5361		
Total	95	94.61			

Table D.43

ANOVA Summary Table for lnHF During Test 3

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	90.65			
Group (A)	1	0.02683	0.02683	0.01	0.9364
Residual between	22	90.62	4.12		
Within subjects	72	115.12			
Time (B)	3	79.21	26.40	51.62	0.0001
A X B Interaction	3	2.15	0.7164	1.40	0.2505
Residual within	66	33.76	0.5115		
Total	95	205.77			

Table D.44

ANOVA Summary Table for lnLF/lnHF During Test 3

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.9463			
Group (A)	1	0.00001534	0.00001534	0.00	0.9851
Residual between	22	0.9463	0.04301		
Within subjects	72	6.60			
Time (B)	3	4.68	1.56	60.65	0.0001
A X B Interaction	3	0.2156	0.0719	2.79	0.0470
Residual within	66	1.70	0.02572		
Total	95	7.54			

Table D.45

ANOVA Summary Table for lnLFNU During Test 3

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	6.32			
Group (A)	1	0.1395	0.1395	0.50	0.4882
Residual between	22	6.18	0.2807		
Within subjects	72	22.46			
Time (B)	3	15.03	5.010	45.63	0.0001
A X B Interaction	3	0.1799	0.05995	0.55	0.6525
Residual within	66	7.2455	0.1098		
Total	95	28.77			

Table D.46

ANOVA Summary Table for lnHFNU During Test 3

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	7.679			
Group (A)	1	0.007168	0.007168	0.02	0.8873
Residual between	22	7.672	0.3487		
Within subjects	72	50.98			
Time (B)	3	37.88	12.63	60.76	0.0001
A X B Interaction	3	1.16	0.3878	2.14	0.1032
Residual within	66	11.94	0.1810		
Total	95	58.66			

Table D.47

ANOVA Summary Table for lnHF/lnTP During Test 3

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.3664			
Group (A)	1	0.002419	0.002419	0.15	0.7059
Residual between	22	0.3640	0.01655		
Within subjects	72	1.38			
Time (B)	3	1.083	0.3609	87.92	0.0001
A X B Interaction	3	0.02760	0.009199	2.24	0.0916
Residual within	66	0.2709	0.004105		
Total	95	1.75			

Table D.48

ANOVA Summary Table for the Mean RR Interval During Test 4

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1661740.8			
Group (A)	1	9341.96	9341.96	0.12	0.7277
Residual between	22	1652398.84	75109.04		
Within subjects	72	1350896.3			
Time (B)	3	1108992.51	369664.17	105.24	0.0001
A X B Interaction	3	10068.51	3356.17	0.96	0.4191
Residual within	66	231835.28	3512.66		
Total	95	3012637.1			

Table D.49

ANOVA Summary Table for SDNN During Test 4

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	64467.1			
Group (A)	1	624.24	624.24	0.22	0.6473
Residual between	22	63842.86	2901.95		
Within subjects	72	40246.63			
Time (B)	3	8275.23	2758.41	5.87	0.0013
A X B Interaction	3	960.20	320.07	0.68	0.5667
Residual within	66	31011.20	469.87		
Total	95	104713.73			

Table D.50

ANOVA Summary Table for lnTP During Test 4

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	39.53			
Group (A)	1	0.02851	0.02851	0.02	0.9009
Residual between	22	39.50	1.80		
Within subjects	72	28.05			
Time (B)	3	4.519	1.506	4.31	0.0077
A X B Interaction	3	0.4717	0.1572	0.45	0.7182
Residual within	66	23.06	0.3494		
Total	95	67.58			

Table D.51

ANOVA Summary Table for lnLF During Test 4

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	49.29			
Group (A)	1	0.1431	0.1431	0.06	0.8026
Residual between	22	49.15	2.23		
Within subjects	72	36.98			
Time (B)	3	7.327	2.44	5.50	0.0020
A X B Interaction	3	0.3491	0.1164	0.26	0.8524
Residual within	66	29.30	0.4439		
Total	95	86.27			

Table D.52

ANOVA Summary Table for lnHF During Test 4

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	73.53			
Group (A)	1	0.6326	0.6326	0.19	0.6664
Residual between	22	72.90	3.31		
Within subjects	72	126.16			
Time (B)	3	78.13	26.04	36.55	0.0001
A X B Interaction	3	0.9999	0.3333	0.47	0.7058
Residual within	66	47.03	0.7126		
Total	95	199.69			

Table D.53

ANOVA Summary Table for lnLF/lnHF During Test 4

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1.40			
Group (A)	1	0.08555	0.08555	1.44	0.2429
Residual between	22	1.31	0.0594		
Within subjects	72	6.618			
Time (B)	3	4.26	1.419	39.94	0.0001
A X B Interaction	3	0.01248	0.004159	0.12	0.9498
Residual within	66	2.346	0.03554		
Total	95	8.01			

Table D.54

ANOVA Summary Table for lnLFNU During Test 4

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	8.42			
Group (A)	1	0.2476	0.2476	0.67	0.4228
Residual between	22	8.17	0.3711		
Within subjects	72	27.79			
Time (B)	3	16.24	5.413	31.25	0.0001
A X B Interaction	3	0.1230	0.04101	0.24	0.8704
Residual within	66	11.43	0.1732		
Total	95	36.21			

Table D.55

ANOVA Summary Table for lnHFNU During Test 4

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	9.45			
Group (A)	1	0.4569	0.4569	1.12	0.3019
Residual between	22	8.994	0.4088		
Within subjects	72	44.01			
Time (B)	3	29.31	9.77	44.15	0.0001
A X B Interaction	3	0.08562	0.02854	0.13	0.9426
Residual within	66	14.61	0.2213		
Total	95	53.46			

Table D.56

ANOVA Summary Table for lnHF/lnTP During Test 4

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.341			
Group (A)	1	0.01628	0.01628	1.10	0.3050
Residual between	22	0.3248	0.01476		
Within subjects	72	1.53			
Time (B)	3	0.9906	0.3302	41.28	0.0001
A X B Interaction	3	0.006508	0.002169	0.27	0.8459
Residual within	66	0.5279	0.007999		
Total	95	1.87			

Table D.57

ANOVA Summary Table for the Mean RR Interval During Test 5

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1486607.4			
Group (A)	1	48732.39	48732.39	0.75	0.3972
Residual between	22	1437875.04	65357.96		
Within subjects	72	1553676.8			
Time (B)	3	1089171.41	363057.14	54.74	0.0001
A X B Interaction	3	26769.76	8923.25	1.35	0.2672
Residual within	66	437735.68	6632.36		
Total	95	3040284.2			

Table D.58

ANOVA Summary Table for SDNN During Test 5

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	68118.05			
Group (A)	1	578.05	578.05	0.19	0.6686
Residual between	22	67540.20	3070.01		
Within subjects	72	57947.49			
Time (B)	3	8550.72	2850.24	3.92	0.0123
A X B Interaction	3	1378.42	549.47	0.63	0.5973
Residual within	66	48018.35	727.55		
Total	95	126065.54			

Table D.59

ANOVA Summary Table for lnTP During Test 5

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	39.07			
Group (A)	1	0.6221	0.6221	0.36	0.5568
Residual between	22	38.45	1.75		
Within subjects	72	22.88			
Time (B)	3	4.27	1.42	5.34	0.0024
A X B Interaction	3	1.005	0.3350	1.26	0.2967
Residual within	66	17.60	0.2667		
Total	95	61.95			

Table D.60

ANOVA Summary Table for lnLF During Test 5

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	43.90			
Group (A)	1	1.305	1.305	0.67	0.4205
Residual between	22	42.59	1.94		
Within subjects	72	28.26			
Time (B)	3	4.304	1.435	4.05	0.0105
A X B Interaction	3	0.6066	0.2022	0.57	0.6358
Residual within	66	23.35	0.3538		
Total	95	72.16			

Table D.61

ANOVA Summary Table for lnHF During Test 5

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	50.74			
Group (A)	1	0.2840	0.2840	0.12	0.7283
Residual between	22	50.46	2.294		
Within subjects	72	73.14			
Time (B)	3	62.33	20.78	44.20	0.0001
A X B Interaction	3	9.79	3.26	6.94	0.0004
Residual within	66	31.02	0.4700		
Total	95	123.88			

Table D.62

ANOVA Summary Table for lnLF/lnHF During Test 5

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.767			
Group (A)	1	0.09991	0.09991	3.30	0.0831
Residual between	22	0.6669	0.0303		
Within subjects	72	3.73			
Time (B)	3	2.218	0.7394	47.55	0.0001
A X B Interaction	3	0.4849	0.1616	10.39	0.0001
Residual within	66	1.0262	0.01555		
Total	95	4.50			

Table D.63

ANOVA Summary Table for lnLFNU During Test 5

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	7.53			
Group (A)	1	0.4956	0.4956	1.55	0.2261
Residual between	22	7.0309	0.3196		
Within subjects	72	29.48			
Time (B)	3	16.82	5.608	33.66	0.0001
A X B Interaction	3	1.6663	0.5554	3.33	0.0246
Residual within	66	10.996	0.1666		
Total	95	37.01			

Table D.64

ANOVA Summary Table for lnHFNU During Test 5

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	7.08			
Group (A)	1	0.9432	0.9432	3.38	0.0796
Residual between	22	6.14	0.2791		
Within subjects	72	32.55			
Time (B)	3	18.67	6.225	41.46	0.0001
A X B Interaction	3	3.968	1.323	8.81	0.0001
Residual within	66	9.9098	0.1501		
Total	95	39.63			

Table D.65

ANOVA Summary Table for lnHF/lnTP During Test 5

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.2351			
Group (A)	1	0.02448	0.02448	2.56	0.1240
Residual between	22	0.2106	0.009571		
Within subjects	72	1.25			
Time (B)	3	0.7404	0.2468	42.80	0.0001
A X B Interaction	3	0.1247	0.04158	7.21	0.0003
Residual within	66	0.3806	0.005767		
Total	95	1.48			

Table D.66

ANOVA Summary Table for SBP During Test 1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	10216.96			
Group (A)	1	135.38	135.38	0.30	0.5922
Residual between	22	10081.58	458.25		
Within subjects	72	2069.01			
Time (B)	3	81.46	27.15	0.91	0.4392
A X B Interaction	3	26.13	8.71	0.29	0.8303
Residual within	66	1961.42	29.72		
Total	95	12285.97			

Table D.67

ANOVA Summary Table for DBP During Test 1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	2688.96			
Group (A)	1	210.04	210.04	1.86	0.1860
Residual between	22	2478.92	112.68		
Within subjects	72	3875.01			
Time (B)	3	2236.46	745.49	30.16	0.0001
A X B Interaction	3	7.13	2.38	0.10	0.9619
Residual within	66	1631.42	24.72		
Total	95	6563.97			

Table D.68

ANOVA Summary Table for MAP During Test 1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	2827.63			
Group (A)	1	183.36	183.36	1.53	0.2298
Residual between	22	2644.27	120.19		
Within subjects	72	2077.31			
Time (B)	3	849.77	283.26	15.30	0.0001
A X B Interaction	3	6.01	2.00	0.11	0.9550
Residual within	66	1221.53	18.51		
Total	95	4904.94			

Table D.69

ANOVA Summary Table for SBP During Test 2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	7619.62			
Group (A)	1	222.04	222.04	0.66	0.4251
Residual between	22	7397.58	336.25		
Within subjects	72	2415.0			
Time (B)	3	505.13	168.38	5.92	0.0012
A X B Interaction	3	33.79	11.26	0.40	0.7561
Residual within	66	1876.08	28.43		
Total	95	10034.62			

Table D.70

ANOVA Summary Table for DBP During Test 2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	3638.0			
Group (A)	1	216.00	216.00	1.39	0.2512
Residual between	22	3422.00	155.55		
Within subjects	72	7258.67			
Time (B)	3	2960.67	986.89	50.18	0.0001
A X B Interaction	3	39.33	13.11	0.67	0.5755
Residual within	66	1298.00	19.67		
Total	95	10896.67			

Table D.71

ANOVA Summary Table for MAP During Test 2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	3848.08			
Group (A)	1	218.00	218.00	1.32	0.2627
Residual between	22	3630.08	165.00		
Within subjects	72	1820.11			
Time (B)	3	851.59	283.86	19.87	0.0001
A X B Interaction	3	25.47	8.49	0.59	0.6211
Residual within	66	943.05	14.29		
Total	95	5668.19			

Table D.72

ANOVA Summary Table for SBP During Test 3

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	9685.34			
Group (A)	1	416.67	416.67	0.99	0.3308
Residual between	22	9268.67	421.3		
Within subjects	72	2002.0			
Time (B)	3	33.33	11.11	0.38	0.7678
A X B Interaction	3	38.67	12.89	0.44	0.7246
Residual within	66	1930.00	24.24		
Total	95	11687.34			

Table D.73

ANOVA Summary Table for DBP During Test 3

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	3397.84			
Group (A)	1	42.67	42.67	0.28	0.6022
Residual between	22	3355.17	152.51		
Within subjects	72	4150.0			
Time (B)	3	2983.50	994.50	59.30	0.0001
A X B Interaction	3	59.67	19.89	1.19	0.3219
Residual within	66	1106.83	16.77		
Total	95	7547.84			

Table D.74

ANOVA Summary Table for MAP During Test 3

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	4643.15			
Group (A)	1	124.42	124.42	0.61	0.4447
Residual between	22	4518.73	205.40		
Within subjects	72	2015.87			
Time (B)	3	1255.50	418.50	38.45	0.0001
A X B Interaction	3	41.94	13.98	1.28	0.2871
Residual within	66	718.43	10.89		
Total	95	6659.02			

Table D.75

ANOVA Summary Table for SBP During Test 4

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	9546.96			
Group (A)	1	84.38	84.38	0.20	0.6622
Residual between	22	9462.58	430.12		
Within subjects	72	2891.0			
Time (B)	3	86.79	28.93	0.71	0.5516
A X B Interaction	3	101.13	33.71	0.82	0.4858
Residual within	66	2703.08	40.96		
Total	95	12437.96			

Table D.76

ANOVA Summary Table for DBP During Test 4

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	4121.34			
Group (A)	1	28.17	28.17	0.15	0.7010
Residual between	22	4093.17	186.05		
Within subjects	72	3772.0			
Time (B)	3	2735.67	911.89	58.57	0.0001
A X B Interaction	3	8.83	2.94	0.19	0.9034
Residual within	66	1027.50	15.57		
Total	95	7893.34			

Table D.77

ANOVA Summary Table for MAP During Test 4

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	4523.22			
Group (A)	1	43.54	43.54	0.21	0.6483
Residual between	22	4479.68	203.62		
Within subjects	72	2044.91			
Time (B)	3	1149.18	383.06	28.30	0.0001
A X B Interaction	3	2.45	0.8154	0.06	0.9805
Residual within	66	893.28	13.53		
Total	95	6568.13			

Table D.78

ANOVA Summary Table for SBP During Test 5

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	10993.63			
Group (A)	1	1305.38	1305.38	2.96	0.0992
Residual between	22	9688.25	440.38		
Within subjects	72	1729.0			
Time (B)	3	204.79	68.26	3.05	0.0346
A X B Interaction	3	47.46	15.82	0.71	0.5512
Residual within	66	1476.75	22.38		
Total	95	12722.63			

Table D.79

ANOVA Summary Table for DBP During Test 5

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	2810.96			
Group (A)	1	126.04	126.04	1.03	0.3206
Residual between	22	2684.92	122.04		
Within subjects	72	4027.0			
Time (B)	3	2800.46	933.49	50.75	0.0001
A X B Interaction	3	12.46	4.15	0.23	0.8782
Residual within	66	1214.08	18.40		
Total	95	6837.96			

Table D.80

ANOVA Summary Table for MAP During Test 5

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	4067.22			
Group (A)	1	381.01	381.01	2.27	0.1458
Residual between	22	3686.21	167.56		
Within subjects	72	1904.22			
Time (B)	3	933.75	311.25	21.36	0.0001
A X B Interaction	3	8.53	2.84	0.20	0.8994
Residual within	66	961.94	14.57		
Total	95	5971.44			

Table D.81

ANOVA Summary Table for Mean RR Interval During PB

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1189423.94			
Group (A)	1	18736.5	18736.5	0.35	0.559
Residual between	22	1170687.44	53213.07		
Within subjects	96	480948.35			
Time (B)	4	36457.54	9114.38	1.84	0.1277
A X B Interaction	4	9351.75	2337.94	0.47	0.7556
Residual within	88	435139.06	4944.76		
Total	119	1670372.29			

Table D.82

ANOVA Summary Table for SDNN During PB

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	150002.87			
Group (A)	1	231.10	231.10	0.03	0.8555
Residual between	22	149771.77	6807.81		
Within subjects	96	28145.63			
Time (B)	4	4214.26	1053.57	4.25	0.0034
A X B Interaction	4	2129.07	532.27	2.15	0.0815
Residual within	88	21802.30	247.75		
Total	119	178148.5			

Table D.83

ANOVA Summary Table for lnTP During PB

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	74.59			
Group (A)	1	0.358	0.358	0.11	0.7476
Residual between	22	74.23	3.37		
Within subjects	96	24.36			
Time (B)	4	0.594	0.149	0.56	0.6897
A X B Interaction	4	0.579	0.145	0.55	0.6999
Residual within	88	23.19	0.264		
Total	119	98.95			

Table D.84

ANOVA Summary Table for lnLF During PB

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	63.10			
Group (A)	1	0.073	0.073	0.03	0.8748
Residual between	22	63.03	2.865		
Within subjects	96	29.48			
Time (B)	4	0.366	0.091	0.29	0.8847
A X B Interaction	4	1.21	0.303	0.96	0.4361
Residual within	88	27.90	0.317		
Total	119	92.58			

Table D.85

ANOVA Summary Table for lnHF During PB

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	128.05			
Group (A)	1	0.187	0.187	0.03	0.8592
Residual between	22	127.86	5.81		
Within subjects	96	34.25			
Time (B)	4	1.533	0.383	1.06	0.3802
A X B Interaction	4	0.965	0.241	0.67	0.6154
Residual within	88	31.75	0.361		
Total	119	162.30			

Table D.86

ANOVA Summary Table for lnLF/lnHF During PB

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.895			
Group (A)	1	0.007	0.007	0.18	0.6776
Residual between	22	0.888	0.04		
Within subjects	96	0.622			
Time (B)	4	0.034	0.008	1.45	0.2244
A X B Interaction	4	0.073	0.018	3.13	0.0187
Residual within	88	0.515	0.006		
Total	119	1.52			

Table D.87

ANOVA Summary Table for lnLFNU During PB

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	30.68			
Group (A)	1	0.015	0.015	0.01	0.9179
Residual between	22	30.66	1.394		
Within subjects	96	14.33			
Time (B)	4	1.26	0.315	2.41	0.055
A X B Interaction	4	1.55	0.388	2.97	0.0238
Residual within	88	11.52	0.131		
Total	119	45.01			

Table D.88

ANOVA Summary Table for lnHFNU During PB

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	4.81			
Group (A)	1	0.082	0.082	0.38	0.5438
Residual between	22	4.73	0.215		
Within subjects	96	3.59			
Time (B)	4	0.152	0.038	1.08	0.3733
A X B Interaction	4	0.333	0.083	2.36	0.0594
Residual within	88	3.10	0.035		
Total	119	8.40			

Table D.89

ANOVA Summary Table for lnHF/lnTP During PB

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.300			
Group (A)	1	0.00003	0.00003	0.00	0.961
Residual between	22	0.29981	0.01362		
Within subjects	96	0.270			
Time (B)	4	0.0146	0.00365	1.43	0.2308
A X B Interaction	4	0.03084	0.007711	3.02	0.022
Residual within	88	0.22463	0.00255269		
Total	119	0.570			

Table D.90

ANOVA Summary Table for Mean RR Interval During SB1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1769894.70			
Group (A)	1	140847.66	140847.66	1.9	0.1817
Residual between	22	1629047.00	74047.59		
Within subjects	96	534379.93			
Time (B)	4	11392.61	2848.15	0.50	0.7361
A X B Interaction	4	21283.87	5320.97	0.93	0.4485
Residual within	88	501703.45	5701.18		
Total	119	2304274.60			

Table D.91

ANOVA Summary Table for SDNN During SB1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	85873.18			
Group (A)	1	1848.60	1848.60	0.48	0.4939
Residual between	22	84024.58	3819.30		
Within subjects	96	23478.40			
Time (B)	4	842.94	210.74	0.84	0.5039
A X B Interaction	4	540.19	135.05	0.54	0.7083
Residual within	88	22095.27	251.08		
Total	119	109351.58			

Table D.92

ANOVA Summary Table for lnTP During SB1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	46.84			
Group (A)	1	2.492	2.492	1.24	0.2782
Residual between	22	44.35	2.015		
Within subjects	96	27.19			
Time (B)	4	0.7834	0.1959	0.68	0.6082
A X B Interaction	4	1.0367	0.2592	0.90	0.4683
Residual within	88	25.37	0.2883		
Total	119	74.03			

Table D.93

ANOVA Summary Table for lnLF During SB1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	74.69			
Group (A)	1	1.488	1.488	0.45	0.5106
Residual between	22	73.20	3.327		
Within subjects	96	40.95			
Time (B)	4	1.154	0.2885	0.65	0.6257
A X B Interaction	4	0.9669	0.2417	0.55	0.7011
Residual within	88	38.83	0.4412		
Total	119	115.64			

Table D.94

ANOVA Summary Table for lnHF During SB1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	85.04			
Group (A)	1	9.658	9.658	2.82	0.1073
Residual between	22	75.38	3.426		
Within subjects	96	33.44			
Time (B)	4	0.7620	0.1904	0.53	0.7112
A X B Interaction	4	1.265	0.3163	0.89	0.4757
Residual within	88	31.41	0.3569		
Total	119	118.48			

Table D.95

ANOVA Summary Table for lnLF/lnHF During SB1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1.1664			
Group (A)	1	0.1600	0.1600	3.50	0.0748
Residual between	22	1.0064	0.04574		
Within subjects	96	1.12			
Time (B)	4	0.01370	0.003424	0.27	0.8942
A X B Interaction	4	0.009518	0.002379	0.19	0.9429
Residual within	88	1.1008	0.01251		
Total	119	2.29			

Table D.96

ANOVA Summary Table for lnLFNU During SB1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	7.848			
Group (A)	1	1.0066	1.0066	3.24	0.0857
Residual between	22	6.8414	0.3110		
Within subjects	96	7.59			
Time (B)	4	0.09474	0.02368	0.28	0.8910
A X B Interaction	4	0.02357	0.005892	0.07	0.9911
Residual within	88	7.4764	0.08496		
Total	119	15.44			

Table D.97

ANOVA Summary Table for lnHFNU During SB1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	12.76			
Group (A)	1	0.7825	0.7825	1.44	0.2433
Residual between	22	11.98	0.5444		
Within subjects	96	11.23			
Time (B)	4	0.1211	0.03027	0.24	0.9142
A X B Interaction	4	0.06760	0.01690	0.13	0.9691
Residual within	88	11.038	0.1254		
Total	119	23.99			

Table D.98

ANOVA Summary Table for lnHF/lnTP During SB1

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.4811			
Group (A)	1	0.06839	0.06839	3.65	0.0694
Residual between	22	0.4127	0.01876		
Within subjects	96	0.3057			
Time (B)	4	0.01152	0.002880	0.88	0.4792
A X B Interaction	4	0.006261	0.001565	0.48	0.7514
Residual within	88	0.2879	0.003271		
Total	119	0.7868			

Table D.99

ANOVA Summary Table for Mean RR Interval During TILT

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1031373.90			
Group (A)	1	18349.17	18349.17	0.40	0.5344
Residual between	22	1013024.71	46046.58		
Within subjects	96	625008.30			
Time (B)	4	10796.79	2699.20	0.39	0.8135
A X B Interaction	4	8994.60	2248.65	0.33	0.8592
Residual within	88	605216.72	6877.46		
Total	119	1656382.20			

Table D.100

ANOVA Summary Table for SDNN During TILT

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	76738.25			
Group (A)	1	1296.79	1296.79	0.38	0.5449
Residual between	22	75441.46	3429.16		
Within subjects	96	27291.23			
Time (B)	4	2008.09	502.02	1.78	0.1403
A X B Interaction	4	445.53	111.38	0.39	0.8120
Residual within	88	24837.61	282.25		
Total	119	104029.48			

Table D.101

ANOVA Summary Table for lnTP During TILT

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	65.16			
Group (A)	1	0.3451	0.3451	0.12	0.7354
Residual between	22	64.81	2.946		
Within subjects	96	25.17			
Time (B)	4	1.8514	0.4628	1.77	0.1412
A X B Interaction	4	0.3593	0.08982	0.34	0.8473
Residual within	88	22.96	0.2609		
Total	119	90.33			

Table D.102

ANOVA Summary Table for lnLF During TILT

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	83.91			
Group (A)	1	0.04157	0.04157	0.01	0.9178
Residual between	22	83.87	3.812		
Within subjects	96	25.44			
Time (B)	4	0.9506	0.2376	0.88	0.4794
A X B Interaction	4	0.7183	0.1796	0.66	0.6180
Residual within	88	23.77	0.2701		
Total	119	109.35			

Table D.103

ANOVA Summary Table for lnHF During TILT

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	122.38			
Group (A)	1	3.002	3.002	0.55	0.4648
Residual between	22	119.38	5.426		
Within subjects	96	165.45			
Time (B)	4	5.197	1.299	3.37	0.0129
A X B Interaction	4	3.952	0.9880	2.56	0.0438
Residual within	88	33.92	0.3855		
Total	119	287.83			

Table D.104

ANOVA Summary Table for lnLF/lnHF During TILT

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	3.91			
Group (A)	1	0.1714	0.1714	1.01	0.3263
Residual between	22	3.7405	0.1700		
Within subjects	96	5.08			
Time (B)	4	0.6387	0.1597	3.61	0.0090
A X B Interaction	4	0.5423	0.1356	3.06	0.0206
Residual within	88	3.8956	0.04427		
Total	119	8.99			

Table D.105

ANOVA Summary Table for lnLFNU During TILT

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1.59			
Group (A)	1	0.1270	0.1270	1.91	0.1811
Residual between	22	1.465	0.06657		
Within subjects	96	2.27			
Time (B)	4	0.4127	0.1032	6.34	0.0002
A X B Interaction	4	0.4238	0.1060	6.51	0.0001
Residual within	88	1.4325	0.01628		
Total	119	3.86			

Table D.106

ANOVA Summary Table for lnHFNU During TILT

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	23.61			
Group (A)	1	1.3747	1.375	1.36	0.2561
Residual between	22	22.24	1.011		
Within subjects	96	35.39			
Time (B)	4	4.1825	1.0456	4.07	0.0045
A X B Interaction	4	4.4062	1.1015	4.29	0.0032
Residual within	88	22.62	0.257		
Total	119	59.01			

Table D.107

ANOVA Summary Table for lnHF/lnTP During TILT

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.8916			
Group (A)	1	0.03454	0.03454	0.89	0.3566
Residual between	22	0.8571	0.03896		
Within subjects	96	0.6508			
Time (B)	4	0.07641	0.01910	3.38	0.0128
A X B Interaction	4	0.07651	0.01912	3.38	0.0127
Residual within	88	0.4979	0.005658		
Total	119	1.542			

Table D.108

ANOVA Summary Table for Mean RR Interval During SB2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	2203039.5			
Group (A)	1	209039.76	209039.76	2.31	0.1431
Residual between	22	1993999.78	90636.35		
Within subjects	96	552252.90			
Time (B)	4	24859.79	6214.95	1.06	0.3833
A X B Interaction	4	9358.85	2339.71	0.40	0.8100
Residual within	88	518034.26	5886.75		
Total	119	2755292.40			

Table D.109

ANOVA Summary Table for SDNN During SB2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	45331.77			
Group (A)	1	199.38	199.38	0.10	0.7582
Residual between	22	45132.39	2051.47		
Within subjects	96	32745.74			
Time (B)	4	1864.40	466.10	1.40	0.2402
A X B Interaction	4	1610.13	402.53	1.21	0.3122
Residual within	88	29271.21	332.63		
Total	119	78077.51			

Table D.110

ANOVA Summary Table for lnTP During SB2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	33.60			
Group (A)	1	0.06499	0.06499	0.04	0.8383
Residual between	22	33.54	1.52		
Within subjects	96	28.35			
Time (B)	4	0.8866	0.2216	0.73	0.5732
A X B Interaction	4	0.7796	0.1949	0.64	0.6334
Residual within	88	26.68	0.3032		
Total	119	61.95			

Table D.111

ANOVA Summary Table for lnLF During SB2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	31.88			
Group (A)	1	0.0008209	0.0008209	0.00	0.9812
Residual between	22	31.88	1.45		
Within subjects	96	34.10			
Time (B)	4	1.933	0.4831	1.33	0.2660
A X B Interaction	4	0.1431	0.03577	0.10	0.9827
Residual within	88	32.02	0.3639		
Total	119	65.98			

Table D.112

ANOVA Summary Table for lnHF During SB2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	41.05			
Group (A)	1	0.7697	0.7697	0.42	0.5235
Residual between	22	40.28	1.831		
Within subjects	96	33.66			
Time (B)	4	1.7531	0.4383	1.22	0.3069
A X B Interaction	4	0.3624	0.0906	0.25	0.9072
Residual within	88	31.54	0.3584		
Total	119	74.71			

Table D.113

ANOVA Summary Table for lnLF/lnHF During SB2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	1.20			
Group (A)	1	0.03310	0.03310	0.62	0.4383
Residual between	22	1.1686	0.05312		
Within subjects	96	0.7720			
Time (B)	4	0.08442	0.02111	2.75	0.0328
A X B Interaction	4	0.01337	0.00334	0.44	0.7820
Residual within	88	0.6742	0.007662		
Total	119	1.974			

Table D.114

ANOVA Summary Table for lnLFNU During SB2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	9.63			
Group (A)	1	0.2345	0.2345	0.55	0.4666
Residual between	22	9.395	0.4271		
Within subjects	96	7.81			
Time (B)	4	0.7099	0.1775	2.25	0.0698
A X B Interaction	4	0.1641	0.0410	0.52	0.7208
Residual within	88	6.934	0.0788		
Total	119	17.44			

Table D.115

ANOVA Summary Table for lnHFNU During SB2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	13.50			
Group (A)	1	0.1779	0.1779	0.29	0.5933
Residual between	22	13.32	0.6055		
Within subjects	96	8.56			
Time (B)	4	0.8497	0.2124	2.47	0.0506
A X B Interaction	4	0.1326	0.03316	0.39	0.8188
Residual within	88	7.577	0.0861		
Total	119	22.06			

Table D.116

ANOVA Summary Table for lnHF/lnTP During SB2

Source	Df	Sum of Squares	Mean Square	F-Value	P-Value
Between subjects	23	0.3922			
Group (A)	1	0.007168	0.007168	0.41	0.5288
Residual between	22	0.3850	0.01750		
Within subjects	96	0.3345			
Time (B)	4	0.01447	0.003620	1.03	0.3952
A X B Interaction	4	0.01147	0.002867	0.82	0.5173
Residual within	88	0.3086	0.003507		
Total	119	0.7267			

Appendix E

Additional Data

Table E.1

HRV Indices During PB Across Time (Mean, sd)

	Group									
	EX					CT				
	T1	T2	T3	T4	T5	T1	T2	T3	T4	T5
Mean RR (ms)	925.88 137.3	923.64 112.6	958.3 100.7	958.33 123.4	985.34 148.6	956.56 105.5	969.42 102.5	998.23 97.2	965.22 161.1	987.06 99.8
SDNN (ms)	74.3 32	77.0 38	91.0 50	91.8 52	99.3 56*	81.7 29	84.3 29	82.9 32	79.4 32	91.1 29*
lnTP ($lnms^2$)	7.43 1.1	7.72 0.8	7.62 1.0	7.74 0.9	7.66 0.9	7.71 0.8	7.70 0.9	7.71 1.2	7.68 0.9	7.92 0.5
lnLF ($lnms^2$)	6.01 0.9	6.03 0.8	6.05 0.8	6.05 0.7	5.87 0.8	6.26 0.6	5.96 1.0	5.97 1.4	5.89 1.2	6.2 0.7
lnHF ($lnms^2$)	6.73 1.1	6.92 1.1	6.81 1.5	6.84 1.4	7.3 1.2	6.99 0.9	7.05 0.9	6.96 1.5	6.95 1.2	7.04 0.9
lnLFNU (ln%)	3.45 0.5	3.29 0.7	3.36 0.7	3.31 0.8	2.89 0.8*	3.43 0.4	3.19 0.5	3.26 0.5	3.19 0.6	3.36 0.5
lnHFNU (ln%)	4.17 0.2	4.17 0.3	4.14 0.3	4.09 0.4	4.32 0.2	4.16 0.3	4.28 0.2	4.25 0.2	4.24 0.2	4.19 0.2
lnLF/ lnHF	0.90 0.1	0.89 0.1	0.91 0.1	0.91 0.2	0.82 0.1*	0.90 0.1	0.85 0.1	0.86 0.1	0.85 0.1	0.89 0.1
LnHF/ lnTP	0.90 0.1	0.89 0.1	0.89 0.1	0.88 0.1	0.95 0.1*	0.91 0.1	0.92 0.1	0.89 0.1	0.90 0.1	0.88 0.1

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
* = $p<0.05$ vs. T1 for respective group
TP = total power
LF = low-frequency power
NU = normalized units
ms = milliseconds

Table E.2

HRV Indices During SB1 Across Time (Mean, sd)

	Group									
	EX					CT				
	T1	T2	T3	T4	T5	T1	T2	T3	T4	T5
Mean RR (ms)	948.3 140	951.8 115	971.8 145	982.9 155	983.2 167	1028.8 124	1051.3 138	1053.5 100	1004.7 156	1042.2 140
SDNN (ms)	72.5 33	77.5 36	78.4 30	85.9 30	79.8 32	85.4 29	89.3 28	83.4 35	87.5 33	87.8 23
lnTP ($lnms^2$)	7.33 0.9	7.59 0.8	7.61 0.7	7.66 0.7	7.58 0.6	7.84 0.7	7.93 0.6	7.65 1.2	7.77 0.8	8.02 0.9
lnLF ($lnms^2$)	6.27 1.2	6.62 0.9	6.43 0.7	6.54 0.9	6.31 0.7	6.71 0.8	6.83 1.0	6.44 1.5	6.58 1.1	6.72 1.1
lnHF ($lnms^2$)	5.8 1.0	6.22 1.0	6.14 1.2	6.03 1.2	5.84 1.2	6.60 0.8	6.66 0.5	6.45 1.2	6.49 0.8	6.66 0.8
lnLFNU (ln%)	4.07 0.2	4.06 0.2	3.99 0.3	4.07 0.3	4.06 0.3	3.88 0.4	3.92 0.4	3.83 0.4	3.88 0.5	3.84 0.5
lnHFNU (ln%)	3.61 0.5	3.66 0.3	3.70 0.5	3.56 0.5	3.59 0.44	3.77 0.5	3.75 0.5	3.84 0.5	3.79 0.4	3.78 0.5
lnLF/ lnHF	1.08 0.1	1.07 0.1	1.07 0.2	1.11 0.2	1.10 0.1	1.03 0.1	1.03 0.1	0.99 0.1	1.02 0.1	1.01 0.1
lnHF/ lnTP	0.79 0.1	0.82 0.1	0.80 0.1	0.78 0.1	0.77 0.1	0.84 0.1	0.84 0.1	0.84 0.1	0.84 0.1	0.83 0.1

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
TP = total power
LF = low-frequency power
NU = normalized units
ms = milliseconds

Table E.3

HRV Indices During TILT Across Time (Mean, sd)

	Group									
	EX					CT				
	T1	T2	T3	T4	T5	T1	T2	T3	T4	T5
Mean RR (ms)	759.7 108	736.0 83	768.2 137	775.4 126	773.2 142	776.2 104	787.0 131	797.7 130	773.6 131	801.7 108
SDNN (ms)	64.4 31	63.5 28	69.4 21	71.6 30	79.7 50	62.1 26	60.7 25	63.8 26	61.3 26	68.0 29
lnTP ($lnms^2$)	7.10 0.9	7.13 0.9	7.48 0.6	7.40 1.1	7.42 1.0	7.16 1.0	7.05 0.8	7.28 0.8	7.15 0.9	7.36 0.9
lnLF ($lnms^2$)	6.51 0.9	6.19 1.0	6.45 0.8	6.42 1.2	6.18 0.9	6.32 1.2	6.22 0.9	6.44 0.8	6.2 1.0	6.38 1.1
lnHF ($lnms^2$)	4.62 1.1	4.58 1.2	4.81 1.2	4.63 1.6	5.58 1.1*	4.62 1.1	4.53 1.3	4.34 1.0	4.52 1.1	4.62 1.0
lnLFNU (ln%)	4.42 0.2	4.40 0.1	4.39 0.2	4.41 0.2	4.12 0.2*	4.39 0.2	4.39 0.2	4.46 0.1	4.40 0.1	4.41 0.1
lnHFNU (ln%)	2.53 0.7	2.78 0.5	2.75 0.6	2.62 0.7	3.52 0.5*	2.69 0.7	2.71 0.6	2.36 0.8	2.72 0.6	2.65 0.6
lnLF/ lnHF	1.46 0.3	1.40 0.2	1.38 0.2	1.48 0.4	1.12 0.1*	1.40 0.2	1.44 0.3	1.54 0.3	1.42 0.3	1.41 0.2
lnHF/ lnTP	0.65 0.1	0.64 0.1	0.64 0.1	0.62 0.2	0.75 0.1*	0.64 0.1	0.63 0.1	0.59 0.1	0.63 0.1	0.62 0.1

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
TP = total power
LF = low-frequency power
NU = normalized units
ms = milliseconds
* = $p<0.05$ vs. T1 for respective group

Table E.4

HRV Indices During SB2 Across Time (Mean, sd)

	Group									
	EX					CT				
	T1	T2	T3	T4	T5	T1	T2	T3	T4	T5
Mean RR (ms)	987.2 160	1009.0 107	1036.2 165	1039.5 166	1025.0 185	1092.9 142	1090.2 142	1123.5 98	1091.5 145	1116.0 159
SDNN (ms)	80.1 21	95.4 32	94.4 31	89.8 25	101.2 30	90.3 19	88.9 14	84.7 31	90.6 25	93.5 27
lnTP ($lnms^2$)	7.56 0.7	7.94 0.8	7.90 0.7	7.82 0.8	7.96 0.6	7.89 0.6	7.94 0.6	7.74 1.1	7.88 0.6	7.96 0.8
lnLF ($lnms^2$)	6.38 0.6	6.83 0.6	6.53 0.6	6.69 0.7	6.58 0.5	6.47 0.8	6.71 0.8	6.50 1.2	6.73 0.6	6.57 0.6
lnHF ($lnms^2$)	6.51 0.7	6.62 1.0	6.59 0.8	6.54 1.0	6.96 0.8	6.75 0.6	6.90 0.6	6.73 1.0	6.72 0.8	6.93 0.7
lnLFNU (ln%)	3.79 0.3	3.94 0.4	3.83 0.3	3.89 0.4	3.63 0.4	3.68 0.5	3.75 0.4	3.73 0.4	3.82 0.4	3.67 0.3
lnHFNU (ln%)	3.93 0.4	3.73 0.4	3.89 0.4	3.75 0.5	4.01 0.4	3.96 0.4	3.94 0.4	3.95 0.6	3.81 0.6	4.03 0.3
lnLF/ lnHF	0.99 0.1	1.05 0.1	1.00 0.1	1.04 0.2	0.96 0.1	0.96 0.1	0.98 0.1	0.97 0.1	1.01 0.2	0.95 0.1
lnHF/ lnTP	0.87 0.1	0.83 0.1	0.83 0.1	0.84 0.1	0.88 0.1	0.86 0.1	0.87 0.1	0.87 0.1	0.85 0.1	0.87 0.1

Mean RR = mean RR interval
TP = total power
SDNN = standard deviation of normal RR intervals
LF = low-frequency power
HF = high-frequency power
NU = normalized units
ln = natural logarithm
ms = milliseconds

Table E.5

Blood Pressure During PB Across Time (Mean, sd)

	Group									
	EX					CT				
	T1	T2	T3	T4	T5	T1	T2	T3	T4	T5
SBP (mmHg)	118.2 11	116.6 8	116.3 10	115.8 13	120.8 10	117.3 12	115.7 13	112.8 11	111.5 9	112.3 10
DBP (mmHg)	76.5 6	76.2 7	75.3 9	75.3 9	74.8 7	74.0 6	73.7 8	73.2 7	75.2 6	73.3 6
MAP (mmHg)	90.4 6	89.7 7	89.0 8	88.8 10	90.2 7	88.4 6	87.7 8	86.4 7	87.3 6	86.3 6

SBP = systolic blood pressure
DBP = diastolic blood pressure
MAP = mean arterial pressure

Table E.6

Blood Pressure During SB1 Across Time (Mean, sd)

	Group									
	EX					CT				
	T1	T2	T3	T4	T5	T1	T2	T3	T4	T5
SBP (mmHg)	117.3 11	117.7 5	116.8 11	112.7 13	120.8 12	115.3 12	113.8 10	112.0 12	111.3 13	111.8 12
DBP (mmHg)	76.8 8	77.0 6	72.8 8	74.2 8	75.3 8	73.0 7.6	71.8 6	73.2 6	72.8 6	72.5 6
MAP (mmHg)	90.3 8	90.5 5	87.5 9	87.0 9	90.5 8	87.1 5	85.8 6	86.1 8	85.7 7	85.6 6

SBP = systolic blood pressure
DBP = diastolic blood pressure
MAP = mean arterial pressure

Table E.7

Blood Pressure During TILT Across Time (Mean, sd)

	Group									
	EX					CT				
	T1	T2	T3	T4	T5	T1	T2	T3	T4	T5
SBP (mmHg)	116.8 11	112.2 6	116.2 11	114.0 10	116.3 13	113.5 12	108.7 12	110.3 12	111.0 12	110.0 11
DBP (mmHg)	87.8 6	88.3 8	87.5 7	86.8 10	87.3 8	84.8 8	85.8 8	84.0 7	85.8 6	85.7 7
MAP (mmHg)	97.5 7	96.3 7	97.0 7	95.9 9	97.0 9	94.4 8	93.4 9	92.8 8	94.2 6	93.8 8

SBP = systolic blood pressure
DBP = diastolic blood pressure
MAP = mean arterial pressure

Table E.8

Blood Pressure During SB2 Across Time (Mean, sd)

	Group									
	EX					CT				
	T1	T2	T3	T4	T5	T1	T2	T3	T4	T5
SBP (mmHg)	118.3 10	116.8 10	114.7 11	113.8 11	119.5 10	115.0 14	113.0 13	112.2 12	115.0 13	113.8 12
DBP (mmHg)	76.7 6.9	74.5 7	71.8 6	74.5 8	75.7 5	74.2 7	72.7 8	71.8 5	72.7 7	72.5 5
MAP (mmHg)	90.5 6	88.6 8	86.1 7	87.6 8	90.3 6	87.8 6	86.1 8	85.3 7	86.8 6	86.2 6

SBP = systolic blood pressure
DBP = diastolic blood pressure
MAP = mean arterial pressure

Table E.9

Descriptive Statistics for the Participants (Mean, sd)

Group	Age (yr)	Height (inches)	Weight (kg)		SSF (mm)		Body Fat (%)		PAQ (kcal•week^{-1})	
			Pre	Post	Pre	Post	Pre	Post	Pre	Post
EX	23.13	69.62	82.616	82.216	136.655	129.351*	18.16	17.26*	1685.8387	3795.0406*
CT	23.14	69.14	79.113	79.113	112.937	111.034*	15.35	15.05*	1704.9428	1721.0419.6

SSF = sum of skinfolds
PAQ = physical activity questionnaire
* = $p<0.05$ vs. pre for respective group

Table E.10

Physiological Indices at Rest and During Peak Exercise (Mean, sd)

Group	VO_2 ($ml \bullet kg^{-1} \bullet min^{-1}$)		VO_2 ($l \bullet min^{-1}$)		V_E ($l \bullet min^{-1}$)		RF ($breaths \bullet min^{-1}$)		V_T ($l \bullet breath^{-1}$)		VCO_2 ($l \bullet min^{-1}$)		RQ		HR ($beats \bullet min^{-1}$)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
EX (Rest)	4.62 1.1	5.36 1.4*	0.38 0.1	0.44 0.2*	15.7 4.1	17.0 4.6*	20.6 4.9	17.9 3.4*	0.88 0.3	1.03 0.3*	0.38 0.1	0.46 0.2*	1.04 0.1	1.07 0.1	83.1 12	83.3 14
CT (Rest)	5.60 1.8	6.44 2.1*	0.43 0.2	0.50 0.2*	15.0 2.5	16.9 4.4*	18.8 3.9	18.2 5.1*	0.88 0.3	1.05 0.3*	0.40 0.1	0.47 0.1*	0.98 0.1‡	0.99 0.1‡	73.5 15	75.7 14
EX (Peak)	33.48 3.7	36.07 3.2*	2.73 0.4	2.92 0.5*	113.3 21	126.6 24*	41.2 8	43.7 8	2.83 0.7	2.98 0.7*	3.62 0.4	3.93 0.7	1.33 0.1	1.35 0.1	184.4 10	185.3 10
CT (Peak)	33.88 3.0	32.65 2.6	2.73 0.6	2.62 0.5	113.6 24	108.5 17	41.4 8	39.8 8	2.82 0.6	2.66 0.6	3.66 0.8	3.44 0.7	1.34 0.1	1.31 0.1	181.2 10	178.9 8

VO_2 = oxygen consumption
V_E = minute ventilation
RF = respiratory frequency
V_T = tidal volume
* = $p<0.05$ vs. pre for respective group
‡ = $p<0.05$ vs. EX
VCO_2 = volume of expired carbon dioxide
RQ = respiratory quotient
HR = heart rate

Table E.11

HRV During Test 1 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
Mean RR (ms)	925.88 137.3	948.3 140	759.7 108*	987.2 160	956.56 105.5†‡	1028.8 124‡	776.2 104*	1092.9 142
SDNN (ms)	74.3 32	72.5 33	64.4 31*	80.1 21	81.7 29	85.4 29	62.1 26*	90.3 19
lnTP ($lnms^2$)	7.43 1.1	7.33 0.9	7.10 0.9*	7.56 0.7	7.71 0.8	7.84 0.7	7.16 1.0*	7.89 0.6
lnLF ($lnms^2$)	6.01 0.9	6.27 1.2	6.51 0.9	6.38 0.6	6.26 0.6	6.71 0.8	6.32 1.2	6.47 0.8
lnHF ($lnms^2$)	6.73 1.1†	5.8 1.0	4.62 1.1*	6.51 0.7†	6.99 0.9†	6.60 0.8	4.62 1.1*	6.75 0.6†
lnLFNU (ln%)	3.45 0.5†‡	4.07 0.2‡	4.42 0.2*	3.79 0.3	3.43 0.4†‡	3.88 0.4‡	4.39 0.2*	3.68 0.5
lnHFNU (ln%)	4.17 0.2†‡	3.61 0.5‡	2.53 0.7*	3.93 0.4	4.16 0.3†‡	3.77 0.5‡	2.69 0.7*	3.96 0.4
lnLF/ lnHF	0.90 0.1†‡	1.08 0.1‡	1.46 0.3*	0.99 0.1	0.90 0.1†‡	1.03 0.1‡	1.40 0.2*	0.96 0.1
lnHF/ lnTP	0.90 0.1†‡	0.79 0.1‡	0.65 0.1*	0.87 0.1	0.91 0.1†‡	0.84 0.1‡	0.64 0.1*	0.86 0.1

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
TP = total power
LF = low-frequency power
NU = normalized units
ms = milliseconds
* = $p<0.05$ vs. other 3 conditions for specified group
† = $p<0.05$ vs. SB1 for specified group
‡ = $p<0.05$ vs. SB2 for specified group

Table E.12

HRV During Test 2 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
Mean RR (ms)	923.64 112.6†‡	951.8 115‡	736.0 83*	1009.0 107	969.42 102.5†‡	1051.3 138‡	787.0 131*	1090.2 142
SDNN (ms)	77.0 38‡	77.5 36	63.5 28*	95.4 32	84.3 29‡	89.3 28	60.7 25*	88.9 14
lnTP ($lnms^2$)	7.72 0.8	7.59 0.8	7.13 0.9*	7.94 0.8	7.70 0.9	7.93 0.6	7.05 0.8*	7.94 0.6
lnLF ($lnms^2$)	6.03 0.8†‡	6.62 0.9	6.19 1.0†‡	6.83 0.6	5.96 1.0†‡	6.83 1.0	6.22 0.9†‡	6.71 0.8
lnHF ($lnms^2$)	6.92 1.1†	6.22 1.0	4.58 1.2*	6.62 1.0†	7.05 0.9†	6.66 0.5	4.53 1.3*	6.90 0.6†
lnLFNU (ln%)	3.29 0.7†‡	4.06 0.2	4.40 0.1*	3.94 0.4	3.19 0.5†‡	3.92 0.4	4.39 0.2*	3.75 0.4
lnHFNU (ln%)	4.17 0.3†‡	3.66 0.3	2.78 0.5*	3.73 0.4	4.28 0.2†‡	3.75 0.5	2.71 0.6*	3.94 0.4
lnLF/ lnHF	0.89 0.1†‡	1.07 0.1	1.40 0.2*	1.05 0.1	0.85 0.1†‡	1.03 0.1	1.44 0.3*	0.98 0.1
lnHF/ lnTP ††	0.89 0.1†‡	0.82 0.1	0.64 0.1*	0.83 0.1	0.92 0.1†‡	0.84 0.1	0.63 0.1*	0.87 0.1

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
TP = total power
LF = low-frequency power
NU = normalized units
ms = milliseconds
* = $p<0.05$ vs. other 3 conditions for specified group
† = $p<0.05$ vs. SB1 for specified group
‡ = $p<0.05$ vs. SB2 for specified group

Table E.13

HRV During Test 3 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
Mean RR (ms)	958.3 100.7‡	971.8 145‡	768.2 137*	1036.2 165	998.23 97.2‡	1053.5 100‡	797.7 130*	1123.5 98
SDNN (ms)	91.0 50	78.4 30	69.4 21*	94.4 31	82.9 32	83.4 35	63.8 26*	84.7 31
lnTP ($lnms^2$)	7.62 1.0	7.61 0.7	7.48 0.6	7.90 0.7	7.71 1.2	7.65 1.2	7.28 0.8	7.74 1.1
lnLF ($lnms^2$)	6.05 0.8	6.43 0.7	6.45 0.8	6.53 0.6	5.97 1.4	6.44 1.5	6.44 0.8	6.50 1.2
lnHF ($lnms^2$)	6.81 1.5†	6.14 1.2	4.81 1.2*	6.59 0.8†	6.96 1.5†	6.45 1.2	4.34 1.0*	6.73 1.0†
lnLFNU (ln%)	3.36 0.7†‡	3.99 0.3	4.39 0.2*	3.83 0.3	3.26 0.5†‡	3.83 0.4	4.46 0.1*	3.73 0.4
lnHFNU (ln%)	4.14 0.3†‡	3.70 0.5	2.75 0.6*	3.89 0.4	4.25 0.2†‡	3.84 0.5	2.36 0.8*	3.95 0.6
lnLF/ lnHF	0.91 0.1†	1.07 0.2	1.38 0.2*	1.00 0.1	0.86 0.1	0.99 0.1	1.54 0.3*	0.97 0.1
lnHF/ lnTP	0.89 0.1†	0.80 0.1	0.64 0.1*	0.83 0.1	0.89 0.1†	0.84 0.1	0.59 0.1*	0.87 0.1

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
TP = total power
LF = low-frequency power
NU = normalized units
ms = milliseconds
* = $p<0.05$ vs. other 3 conditions for specified group
† = $p<0.05$ vs. SB1 for specified group
‡ = $p<0.05$ vs. SB2 for specified group

Table E.14

HRV During Test 4 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
Mean RR (ms)	958.33 123.4‡	982.9 155‡	775.4 126*	1039.5 166	965.22 161.1‡	1004.7 156‡	773.6 131*	1091.5 145
SDNN (ms)	91.8 52	85.9 30	71.6 30*	89.8 25	79.4 32	87.5 33	61.3 26*	90.6 25
lnTP ($lnms^2$)	7.74 0.9	7.66 0.7	7.40 1.1*	7.82 0.8	7.68 0.9	7.77 0.8	7.15 0.9*	7.88 0.6
lnLF ($lnms^2$)	6.05 0.7†‡	6.54 0.9	6.42 1.2	6.69 0.7	5.89 1.2†‡	6.58 1.1	6.2 1.0	6.73 0.6
lnHF ($lnms^2$)	6.84 1.4†	6.03 1.2	4.63 1.6*	6.54 1.0	6.95 1.2†	6.49 0.8	4.52 1.1*	6.72 0.8
lnLFNU (ln%)	3.31 0.8†‡	4.07 0.3	4.41 0.2*	3.89 0.4	3.19 0.6†‡	3.88 0.5	4.40 0.1*	3.82 0.4
lnHFNU (ln%)	4.09 0.4†‡	3.56 0.5	2.62 0.7*	3.75 0.5	4.24 0.2†‡	3.79 0.4	2.72 0.6*	3.81 0.6
lnLF/ lnHF	0.91 0.2†‡	1.11 0.2	1.48 0.4*	1.04 0.2	0.85 0.1†‡	1.02 0.1	1.42 0.3*	1.01 0.2
lnHF/ lnTP	0.88 0.1†	0.78 0.1	0.62 0.2*	0.84 0.1	0.90 0.1†	0.84 0.1	0.63 0.1*	0.85 0.1

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
TP = total power
LF = low-frequency power
NU = normalized units
ms = milliseconds
* = $p<0.05$ vs. other 3 conditions for specified group
† = $p<0.05$ vs. SB1 for specified group
‡ = $p<0.05$ vs. SB2 for specified group

Table E.15

HRV During Test 5 (Mean, sd)

	Group							
	EX				CT			
	PB	SB1	Tilt	SB2	PB	SB1	Tilt	SB2
Mean RR (ms)	985.34 148.6‡	983.2 167‡	773.2 142*	1025.0 185	987.06 99.8‡	1042.2 140‡	801.7 108*	1116.0 159
SDNN (ms)	99.3 56	79.8 32‡	79.7 50‡ϕ	101.2 30	91.1 29	87.8 23‡	68.0 29‡ϕ	93.5 27
lnTP ($lnms^2$)	7.66 0.9	7.58 0.6	7.42 1.0*	7.96 0.6	7.92 0.5	8.02 0.9	7.36 0.9*	7.96 0.8
lnLF ($lnms^2$)	5.87 0.8†‡	6.31 0.7	6.18 0.9	6.58 0.5	6.2 0.7†‡	6.72 1.1	6.38 1.1	6.57 0.6
lnHF ($lnms^2$)	7.3 1.2	5.84 1.2‡ϕ	5.58 1.1‡ϕ	6.96 0.8	7.04 0.9†	6.66 0.8	4.62 1.0*	6.93 0.7
lnLFNU (ln%)	2.89 0.8*	4.06 0.3	4.12 0.2	3.63 0.4	3.36 0.5†	3.84 0.5	4.41 0.1*	3.67 0.3
lnHFNU (ln%)	4.32 0.2	3.59 0.44ϕ	3.52 0.5ϕ	4.01 0.4	4.19 0.2	3.78 0.5	2.65 0.6*	4.03 0.3
lnLF/ lnHF	0.82 0.1	1.10 0.1ϕ	1.12 0.1ϕ	0.96 0.1ϕ	0.89 0.1	1.01 0.1	1.41 0.2*	0.95 0.1
lnHF/ lnTP	0.95 0.1	0.77 0.1‡ϕ	0.75 0.1‡ϕ	0.88 0.1	0.88 0.1	0.83 0.1	0.62 0.1*	0.87 0.1

Mean RR = mean RR interval
SDNN = standard deviation of normal RR intervals
HF = high-frequency power
ln = natural logarithm
TP = total power
LF = low-frequency power
NU = normalized units
* = $p<0.05$ vs. other 3 conditions for specified group
† = $p<0.05$ vs. SB1 for specified group
‡ = $p<0.05$ vs. SB2 for specified group
ϕ = $p<0.05$ vs. PB for specified group

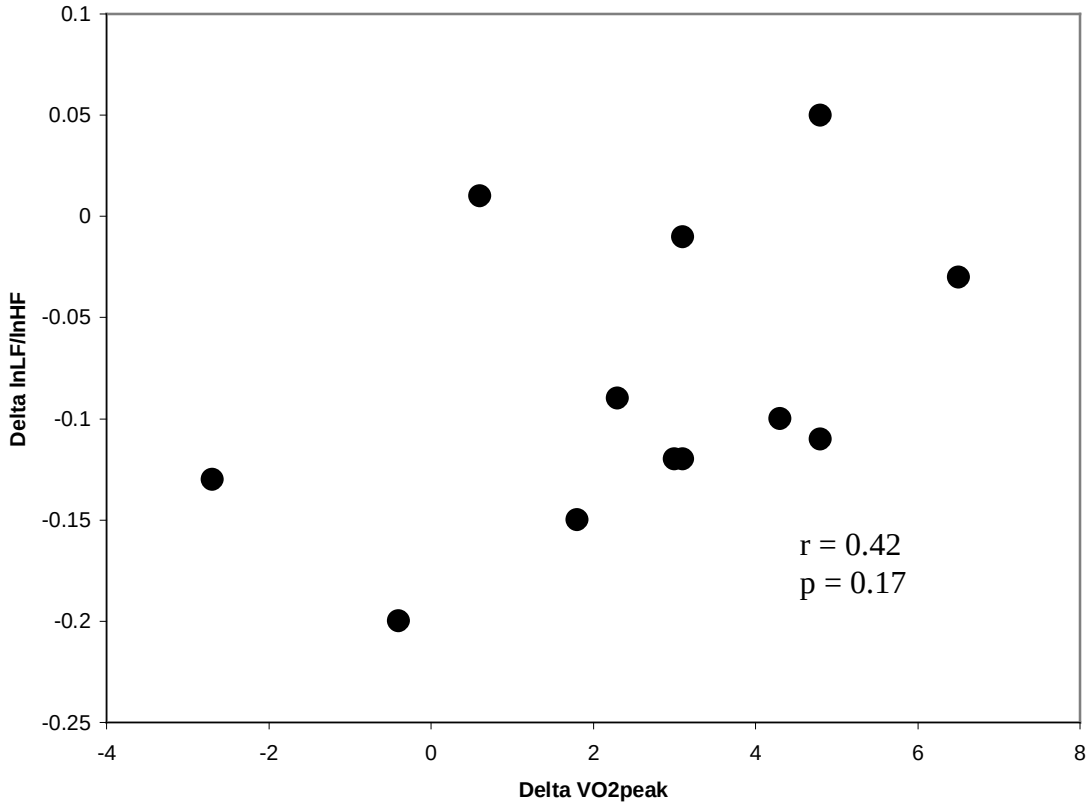

Figure E.1 Relationship Between Delta VO_{2peak} and Delta lnLF/lnHF during PB in EX

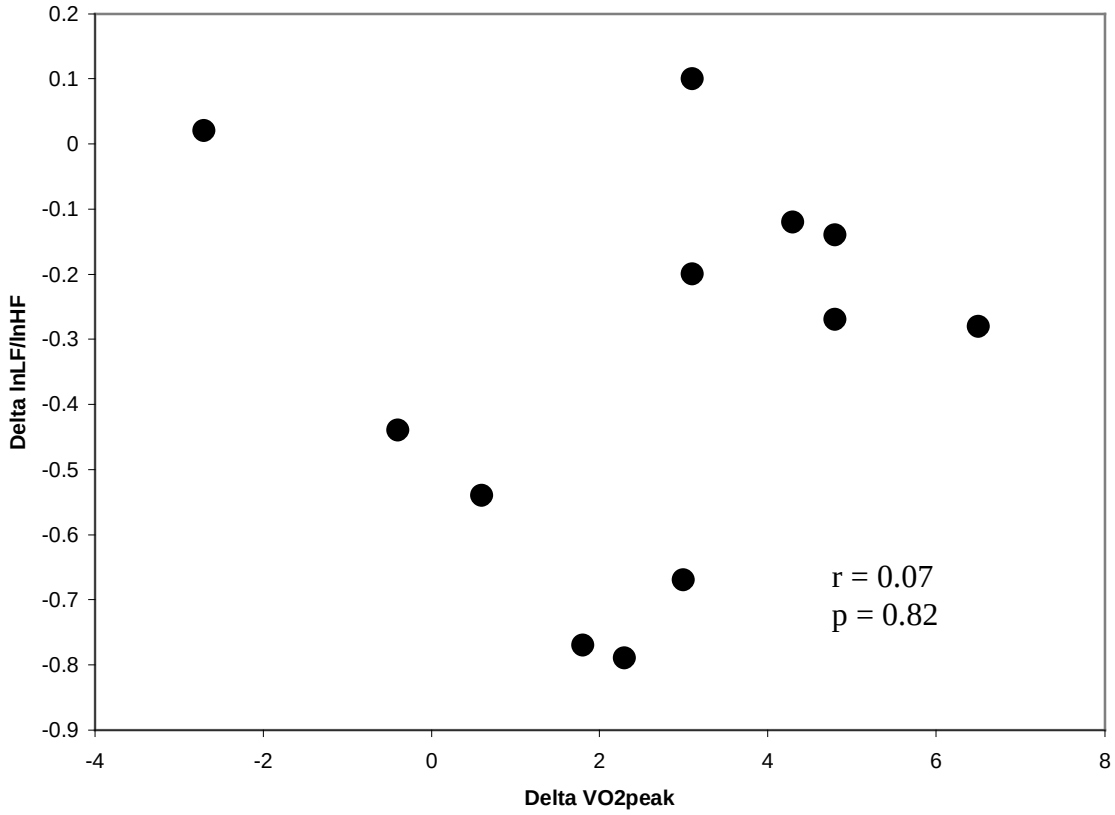

Figure E.2 Relationship Between Delta VO_{2peak} and Delta lnLF/lnHF during TILT in EX

Vita

Clarence Matthew Lee was born on March 15 in the year 1973, in Covington, Louisiana, to Mike and Barbara Lee. He was raised in Baton Rouge, Louisiana, where he attended Lanier Elementary, Istrouma Middle, and Glen Oaks High Schools. Matt then attended the University of Southwestern Louisiana, where he graduated *Magna Cum Laude* in December of the year 1995 and received the degree of Bachelor of Science in Biology, with a minor in Chemistry. He entered the doctoral program at Louisiana State University in 1996, and expects to be awarded the degree of Doctor of Philosophy in December of 2001.

In August of 2001, Matt moved to California to pursue a career in academia. Matt is currently working as a Lecturer, in the Department of Kinesiology at San Francisco State University in San Francisco, California.